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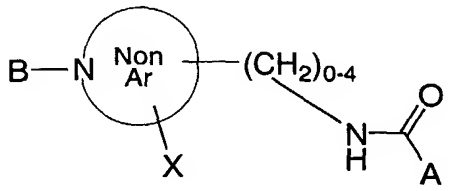
(54) Title: N-SUBSTITUTED NONARYL-HETEROCYCLO AMIDYL NMDA/NR2B ANTAGONISTS



(I)

(57) Abstract: Compounds represented by Formula (I): or pharmaceutically acceptable salts thereof, are effective as NMDA NR2B antagonists useful for relieving pain.

TITLE OF THE INVENTION

N-SUBSTITUTED NONARYL-HETEROCYCLO AMIDYL NMDA/NR2B ANTAGONISTS

BACKGROUND OF THE INVENTION

Field of the Invention

This invention relates to *N*-substituted nonarylheterocyclo amidyl compounds. In particular, this invention relates to *N*-substituted nonarylheterocyclo amidyl compounds that are effective as NMDA NR2B antagonists useful for relieving pain.

Ions such as glutamate play a key role in processes related to chronic pain and pain-associated neurotoxicity – primarily by acting through N-methyl-D-aspartate ("NMDA") receptors. Thus, inhibition of such action – by employing ion channel antagonists, particularly NMDA antagonists – can be beneficial in the treatment and control of pain.

Known NMDA antagonists include ketamine, dextromophan, and 3-(2-carboxypiperazin-4-yl)-propyl-1-phosphonic acid ("CPP"). Although these compounds have been reported (J.D.Kristensen, et al., *Pain*, 51:249-253 (1992); P.K.Eide, et al., *Pain*, 61:221-228 (1995); D.J.Knox, et al., *Anaesth. Intensive Care* 23:620-622 (1995); and M.B.Max, et al., *Clin.Neuropharmacol.* 18:360-368 (1995)) to produce symptomatic relief in a number of neuropathies including postherpetic neuralgia, central pain from spinal cord injury, and phantom limb pain, widespread use of these compounds is precluded by their undesirable side effects. Such side effects at analgesic doses include psychotomimetic effects such as dizziness, headache, hallucinations, dysphoria, and disturbances of cognitive and motor function. Additionally, more severe hallucinations, sedation, and ataxia are produced at doses only marginally higher than analgesic doses. Thus, it would be desirable to provide novel NMDA antagonists that are absent of undesirable side effects or that produce fewer and/or milder side effects.

NMDA receptors are heteromeric assemblies of subunits, of which two major subunit families designated NR1 and NR2 have been cloned. Without being bound by theory, it is generally believed that the various functional NMDA receptors

in the mammalian central nervous system ("CNS") are only formed by combinations of NR1 and NR2 subunits, which respectively express glycine and glutamate recognition sites. The NR2 subunit family is in turn divided into four individual subunit types: NR2A, NR2B, NR2C, and NR2D. T. Ishii, et al., *J. Biol. Chem.*, 268:2836-2843 (1993), and D.J. Laurie et al., *Mol. Brain Res.*, 51:23-32 (1997) describe how the various resulting combinations produce a variety of NMDA receptors differing in physiological and pharmacological properties such as ion gating properties, magnesium sensitivity, pharmacological profile, as well as in anatomical distribution.

For example, while NR1 is found throughout the brain, NR2 subunits are differentially distributed. In particular, it is believed that the distribution map for NR2B lowers the probability of side effects while producing pain relief. For example, S.Boyce, et al., *Neuropharmacology*, 38:611-623(1999) describes the effect of selective NMDA NR2B antagonists on pain with reduced side effects. Thus, it would be desirable to provide novel NMDA antagonists that target the NR2B receptor. Such antagonists would be useful in the treatment of pain, migraine, depression, anxiety, schizophrenia, Parkinson's disease, stroke, glaucoma, or tinitis – maladies that are amenable to amelioration through inhibition of NMDA NR2B receptors.

U.S. Patent No. 6,020,347 and International Patent Publication WO99/25685 describes 4-substituted-4-piperidine carboxamide derivatives that are antagonists of VLA-4 ("Very Late Antigen-4"). International Patent Publication WO 01/00207 describes substituted pyrimidine compounds that are inhibitors of tyrosine kinases. International Patent Publication WO 00/61551 describes oxopyrimidinealkanoate compounds that are integrin receptor ligands. International Patent Publication EP 604800 describes carboxyalkyl-phenyl aminocarbonyl-phenyl-piperidine compounds that are blood platelet aggregation inhibitors. International Patent Publication EP 611660 describes benzimidazoles, xanthines, and analogs as tissue aggregation inhibitors. International Patent Publication EP 771799 and U.S. Patent No 5,861,396 describe purin-6-one derivatives for the treatment of cardiovascular and urogenital diseases. International Patent Publication WO94/21615 describes benzimidazole-piperidine compounds utilized as dopamine D4 antagonists. German Patent No. DE4241632 describes substituted phenyl or cyclohexyl-carboxylic acid derivatives that inhibit cell aggregation.

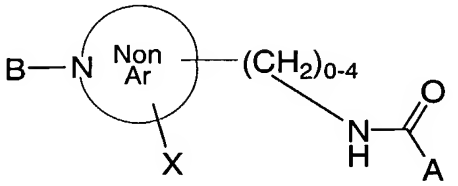
International Patent Publication WO 00/25786 describes heterocyclic potassium channel inhibitors. International Patent Publication WO 00/08015

describes non-peptidic amino derivatives that are follicle stimulating hormone agonists for the treatment of infertility. International Patent Publication WO 98/46589 describes indazole amide compounds as serotoninergic agents. International Patent Publication WO 98/05336 describes compounds that are inhibitors of cysteine protease. International Patent Publication WO 98/04913 describes pharmacophore models of integrin VLA-4 inhibitors. International Patent Publication WO 97/45119 describes the use of substance P antagonists for treating social phobia. International Patent Publication WO 97/28141 describes aromatic piperazines derived from substituted cycloazanes. International Patent Publication WO 97/28139 describes naphthylpiperazines derived from substituted cycloazanes. International Patent Publication WO 96/34856 describes 2-ureido-benzamide derivatives. International Patent Publication WO 96/10035 describes inhibitors of farnesyl-protein transferase. International Patent Publication WO 94/20062 describes balanoids. International Patent Publication WO 94/14776 describes bicyclic fibrinogen antagonists. International Patent Publication EP 532456 describes 1-acylpiperidine derivatives used as substance-P antagonists. International Patent Publication WO/19709 describes imidazolylbenzoyl substituted heterocycles. Japanese Patent Publication JP 10120644 describes 2-ureido-benzamide derivatives for treating ACAT-related diseases. International Patent Publication WO 00/11002 describes 9-dialkylamino purinone derivatives. International Patent Publication WO 98/31669 describes arylpiperazine antidepressants derived from piperidine. International Patent Publication WO 98/31677 describes aromatic amines derived from cyclic amines. R.D. Clark et al., *J.Med. Chem.*, 26:855-861(1983) describes antihypertensive 9-subtituted 1-oxa-4,9-diazaspiro[5.5]undecan-3-ones.

Phenol compounds described as NMDA antagonists are described in U.S. Patent Nos. 5,306,723 and 5,436,255, and in International Patent Publications WO91/17156, WO92/19502, WO93/02052, WO96/37226, and EP 441506. Benzyl piperidine substituted with phenols or imidazoles are described in Z.-L. Zhou, et al., *J. Medicinal Chemistry*, 42:2993-3000(1999); T.F.Gregory, et al., Poster #94, 218th National Meeting American Chemical Society, New Orleans, Louisiana, August 22-26, 1999. Other NMDA NR2B selective compounds are described in European Patent Publication EP 787493 and J.N.C. Kew et al., *British J.Pharmacol.*, 123:463(1998). However, there continues to be a need for novel NMDA antagonists that target the NR2B receptor.

SUMMARY OF THE INVENTION

The present invention relates to *N*-substituted nonarylheterocyclic compounds represented by Formula (I):

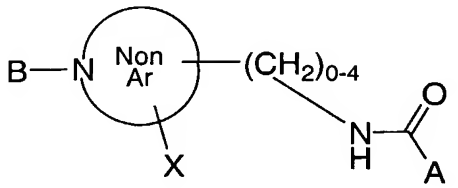


(I)

or pharmaceutically acceptable salts thereof. The present invention also forms pharmaceutical compositions utilizing the compounds. Further, this invention includes novel methods to treat pain by utilizing the compounds.

DETAILED DESCRIPTION OF THE INVENTION

The compounds of this invention are represented by Formula (I):



(I)

or pharmaceutically acceptable salts thereof, wherein

NonAr is a nonaromatic 5-7 membered ring containing a) 1 nitrogen ring atom, b) 2 nitrogen ring atoms, c) 1 nitrogen and 1 oxygen ring atom, or d) 1 nitrogen and 1 sulfur ring atom, wherein the remaining ring atoms are carbon;

A is a phenyl optionally substituted with 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-7}cycloalkyl, -CF_3, halogen, -OH, –CN, imidazolyl, -C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), -O-C_{1-4}alkyl, -C(O)-C_{0-4}alkyl, -C(O)-O-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkylphenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O-C_{1-4}alkyl, or –$NHSO_2$-C_{1-4}alkyl, -O-C_{1-}

4alkylphenyl, or hydroxyiminoethyl; any alkyl optionally substituted with 1-6 –OH or halogen; or

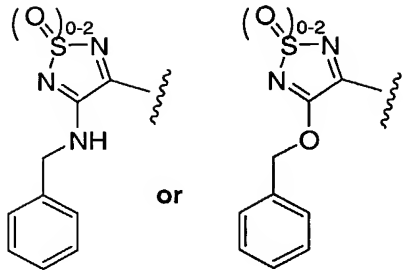
A is pyrrolyl, imidazolyl, pyrazolyl, triazolyl, thiophenyl, thiazolyl, thiadiazolyl, oxazolyl, or isoxazolyl, each optionally substituted with 1-3 substituents, each substituent independently is $-C_{1-4}$alkyl, $-C_{3-7}$cycloalkyl, $-CF_3$, halogen, –OH, –CN, $-C_{1-4}$alkoxyl, phenyl, $-C_{0-4}$alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), $-C_{1-4}$hydroxyalkyl; or

A is pyridyl, pyradazinyl, pyrimidinyl, or pyrazinyl, each optionally substituted with 1-5 substituents; each substituent independently is $-C_{1-4}$alkyl, $-C_{3-7}$cycloalkyl, $-CF_3$, halogen, –OH, –CN, phenyl, pyrrolidinyl, azepanyl, $-C_{1-4}$hydroxyalkyl, $-C_{1-4}$alkoxy, $(CH_3)_2N-(CH_2)_2-NH-$, $-SO_2-C_{1-4}$alkyl, $-C_{0-4}$alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), $-C_{0-4}$alkyl–N(C_{3-6}cycloalkyl)(C_{0-5}alkyl), $-C_{0-4}$alkyl–N(C_{0-5}alkyl)(C_{1-4}alkyloxyC_{1-4}alkyl), –N(C_{0-5}alkyl)–C_{0-4}alkyl-phenyl(C1-4alkoxyl)$_{0-3}$, –N(C_{0-5}alkyl)–C_{0-4}alkylthiaphenyl, dimethoxyphenyl–CH_2–NH–; any phenyl optionally substituted with 1-5 –OH, halogen, or C_{1-4}alkyl; any alkyl optionally substituted with 1-5 –OH or halogen; or the substituent taken with a neighboring bond is =O; or

A is pyrrolophenyl, imidazolophenyl, pyrazolophenyl, triazolophenyl, pyridinoimidazolyl, naphthyridinyl, tetrahydrocyclopentopyrazolyl, quinolinyl, pyrimidinopyrazololyl, benzothiazolyl, benzoimidazolyl, benzoxazolonyl, oxodihydrobenzoxazolyl, indolinonyl, oxadihydroquinolinyl, oxatetrahydroquinolinyl, or purinyl, each optionally substituted with 1-5 substituents, each substituent independently is $-C_{1-4}$alkyl, $-C_{3-7}$cycloalkyl, $-CF_3$, halogen, –OH, or –CN;

B is aryl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, heteroaryl$(CH_2)_{1-3}$–O–$(CH_2)_{0-2}$–C(O)–, indanyl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, aryl$(CH_2)_{1-3}$–C(O)–$(CH_2)_{0-2}$–, aryl–cyclopropyl–C(O)–$(CH_2)_{0-2}$–, heteroaryl$(CH_2)_{1-3}$–C(O)–, aryl$(CH_2)_{1-3}$–, heteroaryl$(CH_2)_{1-3}$–, aryl$(CH_2)_{1-3}$–NH–C(O)–, aryl$(CH_2)_{1-3}$–NH–C(NCN)–, aryl$(CH_2)_{1-3}$–SO_2–, aryl$(CH_2)_{0-3}$–S–$(CH_2)_{0-2}$–C(O)–, or heteroaryl$(CH_2)_{1-3}$–SO_2– wherein any of the aryl or heteroaryl is optionally substituted by 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, phenyl, –O–C_{1-4}alkylphenyl, –S(O)–C_{1-4}alkyl, bromo, fluoro, chloro, or 2 substituents together form methylene dioxy; any (CH_2) optionally is substituted with C_{1-2}alkyl; or

B is



wherein the phenyl is optionally substituted by 1-3 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, bromo, fluoro, or chloro; and

X is H, OH, F, C_{1-4}alkyl, C_{1-4}alkoxy, –N(C_{0-5}alkyl)(C_{0-5}alkyl), phenyl, or =O.

In one aspect, the compounds of this invention are represented by Formula (I) or pharmaceutically acceptable salts thereof, wherein

NonAr is a nonaromatic 6 membered ring containing 1 nitrogen ring atom, wherein the remaining ring atoms are carbon;

A is a phenyl optionally substituted with 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-7}cycloalkyl, -CF_3, halogen, -OH, –CN, imidazolyl, -C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), -O-C_{1-4}alkyl, -C(O)-C_{0-4}alkyl, -C(O)-O-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkylphenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O-C_{1-4}alkyl, or –$NHSO_2$-C_{1-4}alkyl, -O-C_{1-4}alkylphenyl, or hydroxyiminoethyl; any alkyl optionally substituted with 1-6 –OH or halogen; or

A is pyrrolyl, imidazolyl, pyrazolyl, triazolyl, thiophenyl, thiazolyl, thiadiazolyl, oxazolyl, or isoxazolyl, each optionally substituted with 1-3 substituents, each substituent independently is –C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, –CN, -C_{1-4}alkoxyl, phenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), –C_{1-4}hydroxyalkyl; or

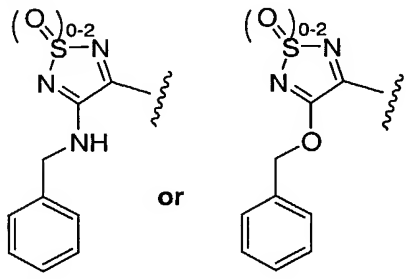
A is pyridyl, pyradazinyl, pyrimidinyl, or pyrazinyl, each optionally substituted with 1-5 substituents; each substituent independently is –C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, –CN, phenyl, pyrrolidinyl, azepanyl, –C_{1-4}hydroxyalkyl, –C_{1-4}alkoxy, $(CH_3)_2N$–$(CH_2)_2$–NH–, -SO_2-C_{1-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), –C_{0-4}alkyl–N(C_{3-6}cycloalkyl)(C_{0-5}alkyl), –C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{1-4}alkyloxyC_{1-4}alkyl), –N(C_{0-5}alkyl)–C_{0-4}alkyl-phenyl(C1-

4alkoxyl)$_{0-3}$, –N(C_{0-5}alkyl)–C_{0-4}alkylthiaphenyl, dimethoxyphenyl–CH_2–NH–; any phenyl optionally substituted with 1-5 –OH, halogen, or C_{1-4}alkyl; any alkyl optionally substituted with 1-5 –OH or halogen; or the substituent taken with a neighboring bond is =O; or

A is pyrrolophenyl, imidazolophenyl, pyrazolophenyl, triazolophenyl, pyridinoimidazolyl, naphthyridinyl, tetrahydrocyclopentopyrazolyl, quinolinyl, pyrimidinopyrazololyl, benzothiazolyl, benzoimidazolyl, benzoxazolonyl, oxodihydrobenzoxazolyl, indolinonyl, oxadihydroquinolinyl, oxatetrahydroquinolinyl, or purinyl, each optionally substituted with 1-5 substituents, each substituent independently is -C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, or –CN;

B is aryl(CH_2)$_{0-3}$–O–(CH_2)$_{0-2}$–C(O)–, heteroaryl(CH_2)$_{1-3}$–O–(CH_2)$_{0-2}$–C(O)–, indanyl(CH_2)$_{0-3}$–O–(CH_2)$_{0-2}$–C(O)–, aryl(CH_2)$_{1-3}$–C(O)–(CH_2)$_{0-2}$–, aryl–cyclopropyl–C(O)–(CH_2)$_{0-2}$–, heteroaryl(CH_2)$_{1-3}$–C(O)–, aryl(CH_2)$_{1-3}$–, heteroaryl(CH_2)$_{1-3}$–, aryl(CH_2)$_{1-3}$–NH–C(O)–, aryl(CH_2)$_{1-3}$–NH–C(NCN)–, aryl(CH_2)$_{1-3}$–SO_2–, aryl(CH_2)$_{0-3}$–S–(CH_2)$_{0-2}$–C(O)–, or heteroaryl(CH_2)$_{1-3}$–SO_2– wherein any of the aryl or heteroaryl is optionally substituted by 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, phenyl, –O–C_{1-4}alkylphenyl, –S(O)–C_{1-4}alkyl, bromo, fluoro, chloro, or 2 substituents together form methylene dioxy; any (CH_2) optionally is substituted with C_{1-2}alkyl; or

B is



wherein the phenyl is optionally substituted by 1-3 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, bromo, fluoro, or chloro; and

X is H, OH, F, C_{1-4}alkyl, C_{1-4}alkoxy, –N(C_{0-5}alkyl)(C_{0-5}alkyl), phenyl, or =O.

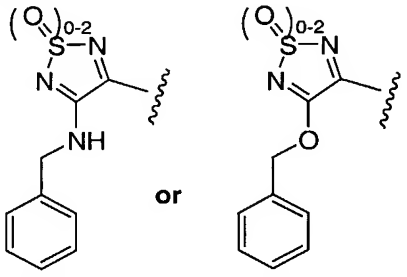
In an embodiment of the first aspect, the compounds of this invention are represented by Formula (I) or pharmaceutically acceptable salts thereof, wherein

NonAr is a nonaromatic 6 membered ring containing 1 nitrogen ring atom, wherein the remaining ring atoms are carbon;

A is a phenyl optionally substituted with 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-7}cycloalkyl, -CF_3, halogen, -OH, –CN, imidazolyl, -C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), -O-C_{1-4}alkyl, -C(O)-C_{0-4}alkyl, -C(O)-O-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkylphenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O-C_{1-4}alkyl, or –$NHSO_2$-C_{1-4}alkyl, -O-C_{1-4}alkylphenyl, or hydroxyiminoethyl; any alkyl optionally substituted with 1-6 –OH or halogen;

B is aryl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, heteroaryl$(CH_2)_{1-3}$–O–$(CH_2)_{0-2}$–C(O)–, indanyl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, aryl$(CH_2)_{1-3}$–C(O)–$(CH_2)_{0-2}$–, aryl–cyclopropyl–C(O)–$(CH_2)_{0-2}$–, heteroaryl$(CH_2)_{1-3}$–C(O)–, aryl$(CH_2)_{1-3}$–, heteroaryl$(CH_2)_{1-3}$–, aryl$(CH_2)_{1-3}$–NH–C(O)–, aryl$(CH_2)_{1-3}$–NH–C(NCN)–, aryl$(CH_2)_{1-3}$–SO_2–, aryl$(CH_2)_{0-3}$–S–$(CH_2)_{0-2}$–C(O)–, or heteroaryl$(CH_2)_{1-3}$–SO_2– wherein any of the aryl or heteroaryl is optionally substituted by 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, phenyl, –O–C_{1-4}alkylphenyl, –S(O)–C_{1-4}alkyl, bromo, fluoro, chloro, or 2 substituents together form methylene dioxy; any (CH_2) optionally is substituted with C_{1-2}alkyl; or

B is



wherein the phenyl is optionally substituted by 1-3 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, bromo, fluoro, or chloro; and

X is H, OH, F, C_{1-4}alkyl, C_{1-4}alkoxy, –N(C_{0-5}alkyl)(C_{0-5}alkyl), phenyl, or =O.

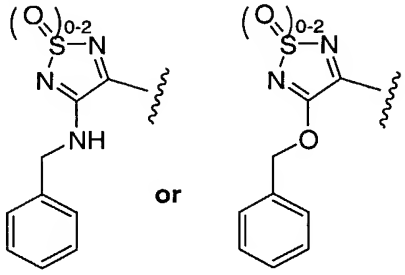
In another aspect of the first aspect, the compounds of this invention are represented by Formula (I) or pharmaceutically acceptable salts thereof, wherein

NonAr is a nonaromatic 6 membered ring containing 1 nitrogen ring atom, wherein the remaining ring atoms are carbon;

A is pyrrolyl, imidazolyl, pyrazolyl, triazolyl, thiophenyl, thiazolyl, thiadiazolyl, oxazolyl, or isoxazolyl, each optionally substituted with 1-3 substituents, each substituent independently is $-C_{1-4}$alkyl, $-C_{3-7}$cycloalkyl, $-CF_3$, halogen, –OH, –CN, $-C_{1-4}$alkoxyl, phenyl, $-C_{0-4}$alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), $-C_{1-4}$hydroxyalkyl;

B is aryl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, heteroaryl$(CH_2)_{1-3}$–O–$(CH_2)_{0-2}$–C(O)–, indanyl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, aryl$(CH_2)_{1-3}$–C(O)–$(CH_2)_{0-2}$–, aryl–cyclopropyl–C(O)–$(CH_2)_{0-2}$–, heteroaryl$(CH_2)_{1-3}$–C(O)–, aryl$(CH_2)_{1-3}$–, heteroaryl$(CH_2)_{1-3}$–, aryl$(CH_2)_{1-3}$–NH–C(O)–, aryl$(CH_2)_{1-3}$–NH–C(NCN)–, aryl$(CH_2)_{1-3}$–SO_2–, aryl$(CH_2)_{0-3}$–S–$(CH_2)_{0-2}$–C(O)–, or heteroaryl$(CH_2)_{1-3}$–SO_2– wherein any of the aryl or heteroaryl is optionally substituted by 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, phenyl, –O–C_{1-4}alkylphenyl, –S(O)–C_{1-4}alkyl, bromo, fluoro, chloro, or 2 substituents together form methylene dioxy; any (CH_2) optionally is substituted with C_{1-2}alkyl; or

B is



wherein the phenyl is optionally substituted by 1-3 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, bromo, fluoro, or chloro; and

X is H, OH, F, C_{1-4}alkyl, C_{1-4}alkoxy, –N(C_{0-5}alkyl)(C_{0-5}alkyl), phenyl, or =O.

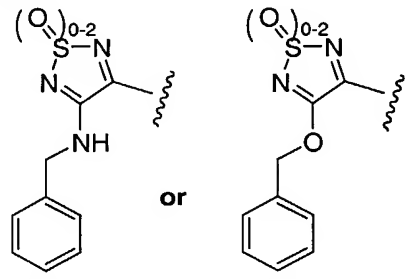
In still another embodiment of the first aspect, the compounds of this invention are represented by Formula (I) or pharmaceutically acceptable salts thereof, wherein

NonAr is a nonaromatic 6 membered ring containing 1 nitrogen ring atom, wherein the remaining ring atoms are carbon;

A is pyridyl, pyradazinyl, pyrimidinyl, or pyrazinyl, each optionally substituted with 1-5 substituents; each substituent independently is –C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, –CN, phenyl, pyrrolidinyl, azepanyl, –C_{1-4}hydroxyalkyl, –C_{1-4}alkoxy, $(CH_3)_2N$–$(CH_2)_2$–NH–, -SO_2-C_{1-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), –C_{0-4}alkyl–N(C_{3-6}cycloalkyl)(C_{0-5}alkyl), –C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{1-4}alkyloxyC_{1-4}alkyl), –N(C_{0-5}alkyl)–C_{0-4}alkyl-phenyl(C1-4alkoxyl)$_{0-3}$, –N(C_{0-5}alkyl)–C_{0-4}alkylthiaphenyl, dimethoxyphenyl–CH_2–NH–; any phenyl optionally substituted with 1-5 –OH, halogen, or C_{1-4}alkyl; any alkyl optionally substituted with 1-5 –OH or halogen; or the substituent taken with a neighboring bond is =O;

B is aryl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, heteroaryl$(CH_2)_{1-3}$–O–$(CH_2)_{0-2}$–C(O)–, indanyl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, aryl$(CH_2)_{1-3}$–C(O)–$(CH_2)_{0-2}$–, aryl–cyclopropyl–C(O)–$(CH_2)_{0-2}$–, heteroaryl$(CH_2)_{1-3}$–C(O)–, aryl$(CH_2)_{1-3}$–, heteroaryl$(CH_2)_{1-3}$–, aryl$(CH_2)_{1-3}$–NH–C(O)–, aryl$(CH_2)_{1-3}$–NH–C(NCN)–, aryl$(CH_2)_{1-3}$–SO_2–, aryl$(CH_2)_{0-3}$–S–$(CH_2)_{0-2}$–C(O)–, or heteroaryl$(CH_2)_{1-3}$–SO_2– wherein any of the aryl or heteroaryl is optionally substituted by 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, phenyl, –O–C_{1-4}alkylphenyl, –S(O)–C_{1-4}alkyl, bromo, fluoro, chloro, or 2 substituents together form methylene dioxy; any (CH_2) optionally is substituted with C_{1-2}alkyl; or

B is



wherein the phenyl is optionally substituted by 1-3 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, bromo, fluoro, or chloro; and

X is H, OH, F, C_{1-4}alkyl, C_{1-4}alkoxy, –N(C_{0-5}alkyl)(C_{0-5}alkyl), phenyl, or =O.

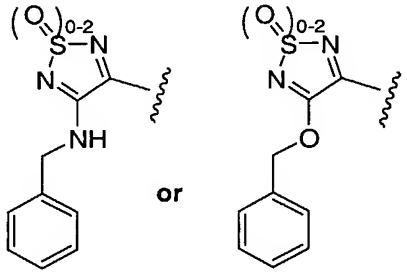
In another embodiment of the first aspect, the compounds of this invention are represented by Formula (I) or pharmaceutically acceptable salts thereof, wherein

NonAr is a nonaromatic 6 membered ring containing 1 nitrogen ring atom, wherein the remaining ring atoms are carbon;

A is pyrrolophenyl, imidazolophenyl, pyrazolophenyl, triazolophenyl, pyridinoimidazolyl, naphthyridinyl, tetrahydrocyclopentopyrazolyl, quinolinyl, pyrimidinopyrazololyl, benzothiazolyl, benzoimidazolyl, benzoxazolonyl, oxodihydrobenzoxazolyl, indolinonyl, oxadihydroquinolinyl, oxatetrahydroquinolinyl, or purinyl, each optionally substituted with 1-5 substituents, each substituent independently is -C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, or –CN;

B is aryl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, heteroaryl$(CH_2)_{1-3}$–O–$(CH_2)_{0-2}$–C(O)–, indanyl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, aryl$(CH_2)_{1-3}$–C(O)–$(CH_2)_{0-2}$–, aryl–cyclopropyl–C(O)–$(CH_2)_{0-2}$–, heteroaryl$(CH_2)_{1-3}$–C(O)–, aryl$(CH_2)_{1-3}$–, heteroaryl$(CH_2)_{1-3}$–, aryl$(CH_2)_{1-3}$–NH–C(O)–, aryl$(CH_2)_{1-3}$–NH–C(NCN)–, aryl$(CH_2)_{1-3}$–SO_2–, aryl$(CH_2)_{0-3}$–S–$(CH_2)_{0-2}$–C(O)–, or heteroaryl$(CH_2)_{1-3}$–SO_2– wherein any of the aryl or heteroaryl is optionally substituted by 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, phenyl, –O–C_{1-4}alkylphenyl, –S(O)–C_{1-4}alkyl, bromo, fluoro, chloro, or 2 substituents together form methylene dioxy; any (CH_2) optionally is substituted with C_{1-2}alkyl; or

B is



wherein the phenyl is optionally substituted by 1-3 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, bromo, fluoro, or chloro; and

X is H, OH, F, C_{1-4}alkyl, C_{1-4}alkoxy, –N(C_{0-5}alkyl)(C_{0-5}alkyl), phenyl, or =O.

In a second aspect, the compounds of this invention are represented by Formula (I) or pharmaceutically acceptable salts thereof, wherein

NonAr is a nonaromatic 5 membered ring containing 1 nitrogen ring atom, wherein the remaining ring atoms are carbon;

A is a phenyl optionally substituted with 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-7}cycloalkyl, -CF_3, halogen, -OH, –CN, imidazolyl, -C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), -O-C_{1-4}alkyl, -C(O)-C_{0-4}alkyl, -C(O)-O-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkylphenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O-C_{1-4}alkyl, or –$NHSO_2$-C_{1-4}alkyl, -O-C_{1-4}alkylphenyl, or hydroxyiminoethyl; any alkyl optionally substituted with 1-6 –OH or halogen; or

A is pyrrolyl, imidazolyl, pyrazolyl, triazolyl, thiophenyl, thiazolyl, thiadiazolyl, oxazolyl, or isoxazolyl, each optionally substituted with 1-3 substituents, each substituent independently is –C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, –CN, -C_{1-4}alkoxyl, phenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), –C_{1-4}hydroxyalkyl; or

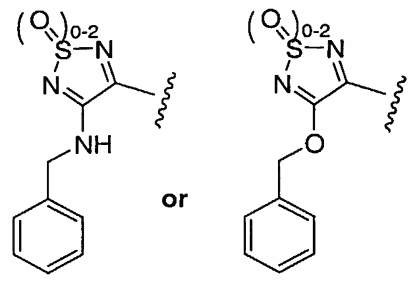
A is pyridyl, pyradazinyl, pyrimidinyl, or pyrazinyl, each optionally substituted with 1-5 substituents; each substituent independently is –C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, –CN, phenyl, pyrrolidinyl, azepanyl, –C_{1-4}hydroxyalkyl, –C_{1-4}alkoxy, $(CH_3)_2N$–$(CH_2)_2$–NH–, -SO_2-C_{1-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), –C_{0-4}alkyl–N(C_{3-6}cycloalkyl)(C_{0-5}alkyl), –C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{1-4}alkyloxyC_{1-4}alkyl), –N(C_{0-5}alkyl)–C_{0-4}alkyl-phenyl(C1-4alkoxyl)$_{0-3}$, –N(C_{0-5}alkyl)–C_{0-4}alkylthiaphenyl, dimethoxyphenyl–CH_2–NH–; any phenyl optionally substituted with 1-5 –OH, halogen, or C_{1-4}alkyl; any alkyl optionally substituted with 1-5 –OH or halogen; or the substituent taken with a neighboring bond is =O; or

A is pyrrolophenyl, imidazolophenyl, pyrazolophenyl, triazolophenyl, pyridinoimidazolyl, naphthyridinyl, tetrahydrocyclopentopyrazolyl, quinolinyl, pyrimidinopyrazololyl, benzothiazolyl, benzoimidazolyl, benzoxazolonyl, oxodihydrobenzoxazolyl, indolinonyl, oxadihydroquinolinyl, oxatetrahydroquinolinyl, or purinyl, each optionally substituted with 1-5 substituents, each substituent independently is -C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, or –CN;

B is aryl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, heteroaryl$(CH_2)_{1-3}$–O–$(CH_2)_{0-2}$–C(O)–, indanyl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, aryl$(CH_2)_{1-3}$–C(O)–$(CH_2)_{0-2}$–, aryl–

cyclopropyl–C(O)–$(CH_2)_{0-2}$–, heteroaryl$(CH_2)_{1-3}$–C(O)–, aryl$(CH_2)_{1-3}$–, heteroaryl$(CH_2)_{1-3}$–, aryl$(CH_2)_{1-3}$–NH–C(O)–, aryl$(CH_2)_{1-3}$–NH–C(NCN)–, aryl$(CH_2)_{1-3}$–SO_2–, aryl$(CH_2)_{0-3}$–S–$(CH_2)_{0-2}$–C(O)–, or heteroaryl$(CH_2)_{1-3}$–SO_2– wherein any of the aryl or heteroaryl is optionally substituted by 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, phenyl, –O–C_{1-4}alkylphenyl, –S(O)–C_{1-4}alkyl, bromo, fluoro, chloro, or 2 substituents together form methylene dioxy; any (CH_2) optionally is substituted with C_{1-2}alkyl; or

B is



wherein the phenyl is optionally substituted by 1-3 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, bromo, fluoro, or chloro; and

X is H, OH, F, C_{1-4}alkyl, C_{1-4}alkoxy, –N(C_{0-5}alkyl)(C_{0-5}alkyl), phenyl, or =O.

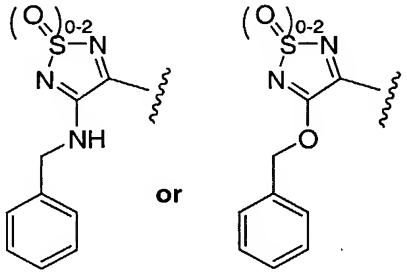
In an embodiment of the second aspect, the compounds of this invention are represented by Formula (I) or pharmaceutically acceptable salts thereof, wherein

NonAr is a nonaromatic 5 membered ring containing 1 nitrogen ring atom, wherein the remaining ring atoms are carbon;

A is a phenyl optionally substituted with 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-7}cycloalkyl, -CF_3, halogen, -OH, –CN, imidazolyl, -C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), -O-C_{1-4}alkyl, -C(O)-C_{0-4}alkyl, -C(O)-O-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkylphenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O-C_{1-4}alkyl, or –$NHSO_2$-C_{1-4}alkyl, -O-C_{1-4}alkylphenyl, or hydroxyiminoethyl; any alkyl optionally substituted with 1-6 –OH or halogen;

B is aryl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, heteroaryl$(CH_2)_{1-3}$–O–$(CH_2)_{0-2}$–C(O)–, indanyl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, aryl$(CH_2)_{1-3}$–C(O)–$(CH_2)_{0-2}$–, aryl–cyclopropyl–C(O)–$(CH_2)_{0-2}$–, heteroaryl$(CH_2)_{1-3}$–C(O)–, aryl$(CH_2)_{1-3}$–, heteroaryl$(CH_2)_{1-3}$–, aryl$(CH_2)_{1-3}$–NH–C(O)–, aryl$(CH_2)_{1-3}$–NH–C(NCN)–, aryl$(CH_2)_{1-3}$–SO_2–, aryl$(CH_2)_{0-3}$–S–$(CH_2)_{0-2}$–C(O)–, or heteroaryl$(CH_2)_{1-3}$–SO_2– wherein any of the aryl or heteroaryl is optionally substituted by 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, phenyl, –O–C_{1-4}alkylphenyl, –S(O)–C_{1-4}alkyl, bromo, fluoro, chloro, or 2 substituents together form methylene dioxy; any (CH_2) optionally is substituted with C_{1-2}alkyl; or

B is



wherein the phenyl is optionally substituted by 1-3 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, bromo, fluoro, or chloro; and

X is H, OH, F, C_{1-4}alkyl, C_{1-4}alkoxy, –N(C_{0-5}alkyl)(C_{0-5}alkyl), phenyl, or =O.

In a third aspect, the compounds of this invention are represented by Formula (I) or pharmaceutically acceptable salts thereof, wherein

NonAr is a nonaromatic 6 membered ring containing 2 nitrogen ring atoms, wherein the remaining ring atoms are carbon;

A is a phenyl optionally substituted with 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-7}cycloalkyl, -CF_3, halogen, -OH, –CN, imidazolyl, -C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), -O-C_{1-4}alkyl, -C(O)-C_{0-4}alkyl, -C(O)-O-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkylphenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O-C_{1-4}alkyl, or –$NHSO_2$-C_{1-4}alkyl, -O-C_{1-4}alkylphenyl, or hydroxyiminoethyl; any alkyl optionally substituted with 1-6 –OH or halogen; or

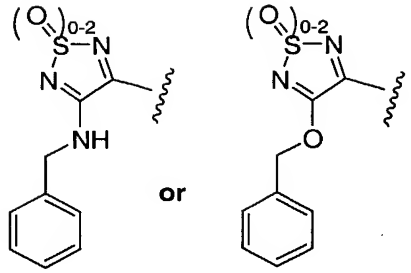
A is pyrrolyl, imidazolyl, pyrazolyl, triazolyl, thiophenyl, thiazolyl, thiadiazolyl, oxazolyl, or isoxazolyl, each optionally substituted with 1-3 substituents, each substituent independently is –C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, –CN, -C_{1-4}alkoxyl, phenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), –C_{1-4}hydroxyalkyl; or

A is pyridyl, pyradazinyl, pyrimidinyl, or pyrazinyl, each optionally substituted with 1-5 substituents; each substituent independently is –C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, –CN, phenyl, pyrrolidinyl, azepanyl, –C_{1-4}hydroxyalkyl, –C_{1-4}alkoxy, $(CH_3)_2N$–$(CH_2)_2$–NH–, -SO_2-C_{1-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), –C_{0-4}alkyl–N(C_{3-6}cycloalkyl)(C_{0-5}alkyl), –C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{1-4}alkyloxyC_{1-4}alkyl), –N(C_{0-5}alkyl)–C_{0-4}alkyl-phenyl(C_{1-4}alkoxyl)$_{0-3}$, –N(C_{0-5}alkyl)–C_{0-4}alkylthiaphenyl, dimethoxyphenyl–CH_2–NH–; any phenyl optionally substituted with 1-5 –OH, halogen, or C_{1-4}alkyl; any alkyl optionally substituted with 1-5 –OH or halogen; or the substituent taken with a neighboring bond is =O; or

A is pyrrolophenyl, imidazolophenyl, pyrazolophenyl, triazolophenyl, pyridinoimidazolyl, naphthyridinyl, tetrahydrocyclopentopyrazolyl, quinolinyl, pyrimidinopyrazololyl, benzothiazolyl, benzoimidazolyl, benzoxazolonyl, oxodihydrobenzoxazolyl, indolinonyl, oxadihydroquinolinyl, oxatetrahydroquinolinyl, or purinyl, each optionally substituted with 1-5 substituents, each substituent independently is -C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, or –CN;

B is aryl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, heteroaryl$(CH_2)_{1-3}$–O–$(CH_2)_{0-2}$–C(O)–, indanyl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, aryl$(CH_2)_{1-3}$–C(O)–$(CH_2)_{0-2}$–, aryl–cyclopropyl–C(O)–$(CH_2)_{0-2}$–, heteroaryl$(CH_2)_{1-3}$–C(O)–, aryl$(CH_2)_{1-3}$–, heteroaryl$(CH_2)_{1-3}$–, aryl$(CH_2)_{1-3}$–NH–C(O)–, aryl$(CH_2)_{1-3}$–NH–C(NCN)–, aryl$(CH_2)_{1-3}$–SO_2–, aryl$(CH_2)_{0-3}$–S–$(CH_2)_{0-2}$–C(O)–, or heteroaryl$(CH_2)_{1-3}$–SO_2– wherein any of the aryl or heteroaryl is optionally substituted by 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, phenyl, –O–C_{1-4}alkylphenyl, –S(O)–C_{1-4}alkyl, bromo, fluoro, chloro, or 2 substituents together form methylene dioxy; any (CH_2) optionally is substituted with C_{1-2}alkyl; or

B is



wherein the phenyl is optionally substituted by 1-3 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, bromo, fluoro, or chloro; and

X is H, OH, F, C_{1-4}alkyl, C_{1-4}alkoxy, –N(C_{0-5}alkyl)(C_{0-5}alkyl), phenyl, or =O.

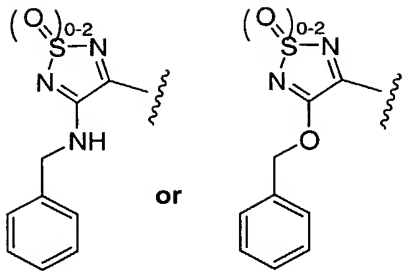
In an embodiment of the third aspect, the compounds of this invention are represented by Formula (I) or pharmaceutically acceptable salts thereof, wherein

NonAr is a nonaromatic 6 membered ring containing 2 nitrogen ring atoms, wherein the remaining ring atoms are carbon;

A is a phenyl optionally substituted with 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-7}cycloalkyl, -CF_3, halogen, -OH, –CN, imidazolyl, -C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), -O-C_{1-4}alkyl, -C(O)-C_{0-4}alkyl, -C(O)-O-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkylphenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O-C_{1-4}alkyl, or –$NHSO_2$-C_{1-4}alkyl, -O-C_{1-4}alkylphenyl, or hydroxyiminoethyl; any alkyl optionally substituted with 1-6 –OH or halogen;

B is aryl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, heteroaryl$(CH_2)_{1-3}$–O–$(CH_2)_{0-2}$–C(O)–, indanyl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, aryl$(CH_2)_{1-3}$–C(O)–$(CH_2)_{0-2}$–, aryl–cyclopropyl–C(O)–$(CH_2)_{0-2}$–, heteroaryl$(CH_2)_{1-3}$–C(O)–, aryl$(CH_2)_{1-3}$–, heteroaryl$(CH_2)_{1-3}$–, aryl$(CH_2)_{1-3}$–NH–C(O)–, aryl$(CH_2)_{1-3}$–NH–C(NCN)–, aryl$(CH_2)_{1-3}$–SO_2–, aryl$(CH_2)_{0-3}$–S–$(CH_2)_{0-2}$–C(O)–, or heteroaryl$(CH_2)_{1-3}$–SO_2– wherein any of the aryl or heteroaryl is optionally substituted by 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, phenyl, –O–C_{1-4}alkylphenyl, –S(O)–C_{1-4}alkyl, bromo, fluoro, chloro, or 2 substituents together form methylene dioxy; any (CH_2) optionally is substituted with C_{1-2}alkyl; or

B is



wherein the phenyl is optionally substituted by 1-3 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, bromo, fluoro, or chloro; and

X is H, OH, F, C_{1-4}alkyl, C_{1-4}alkoxy, –N(C_{0-5}alkyl)(C_{0-5}alkyl), phenyl, or =O.

In a fourth aspect, the compounds of this invention are represented by Formula (I) or pharmaceutically acceptable salts thereof, wherein

NonAr is a nonaromatic 6 membered ring containing 1 nitrogen ring atom and 1 oxygen ring atom, wherein the remaining ring atoms are carbon;

A is a phenyl optionally substituted with 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-7}cycloalkyl, -CF_3, halogen, -OH, –CN, imidazolyl, -C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), -O-C_{1-4}alkyl, -C(O)-C_{0-4}alkyl, -C(O)-O-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkylphenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O-C_{1-4}alkyl, or –$NHSO_2$-C_{1-4}alkyl, -O-C_{1-4}alkylphenyl, or hydroxyiminoethyl; any alkyl optionally substituted with 1-6 –OH or halogen; or

A is pyrrolyl, imidazolyl, pyrazolyl, triazolyl, thiophenyl, thiazolyl, thiadiazolyl, oxazolyl, or isoxazolyl, each optionally substituted with 1-3 substituents, each substituent independently is –C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, –CN, -C_{1-4}alkoxyl, phenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), –C_{1-4}hydroxyalkyl; or

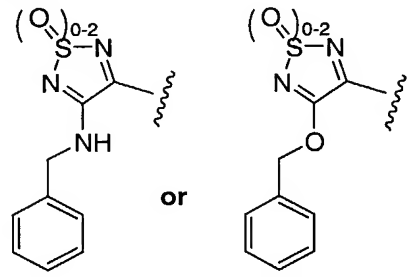
A is pyridyl, pyradazinyl, pyrimidinyl, or pyrazinyl, each optionally substituted with 1-5 substituents; each substituent independently is –C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, –CN, phenyl, pyrrolidinyl, azepanyl, –C_{1-4}hydroxyalkyl, –C_{1-4}alkoxy, $(CH_3)_2N$–$(CH_2)_2$–NH–, -SO_2-C_{1-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), –C_{0-4}alkyl–N(C_{3-6}cycloalkyl)(C_{0-5}alkyl), –C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{1-4}alkyloxyC_{1-4}alkyl), –N(C_{0-5}alkyl)–C_{0-4}alkyl-phenyl(C1-

4alkoxyl)$_{0-3}$, –N(C_{0-5}alkyl)–C_{0-4}alkylthiaphenyl, dimethoxyphenyl–CH_2–NH–; any phenyl optionally substituted with 1-5 –OH, halogen, or C_{1-4}alkyl; any alkyl optionally substituted with 1-5 –OH or halogen; or the substituent taken with a neighboring bond is =O; or

A is pyrrolophenyl, imidazolophenyl, pyrazolophenyl, triazolophenyl, pyridinoimidazolyl, naphthyridinyl, tetrahydrocyclopentopyrazolyl, quinolinyl, pyrimidinopyrazololyl, benzothiazolyl, benzoimidazolyl, benzoxazolonyl, oxodihydrobenzoxazolyl, indolinonyl, oxadihydroquinolinyl, oxatetrahydroquinolinyl, or purinyl, each optionally substituted with 1-5 substituents, each substituent independently is -C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, or –CN;

B is aryl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, heteroaryl$(CH_2)_{1-3}$–O–$(CH_2)_{0-2}$–C(O)–, indanyl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, aryl$(CH_2)_{1-3}$–C(O)–$(CH_2)_{0-2}$–, aryl–cyclopropyl–C(O)–$(CH_2)_{0-2}$–, heteroaryl$(CH_2)_{1-3}$–C(O)–, aryl$(CH_2)_{1-3}$–, heteroaryl$(CH_2)_{1-3}$–, aryl$(CH_2)_{1-3}$–NH–C(O)–, aryl$(CH_2)_{1-3}$–NH–C(NCN)–, aryl$(CH_2)_{1-3}$–SO_2–, aryl$(CH_2)_{0-3}$–S–$(CH_2)_{0-2}$–C(O)–, or heteroaryl$(CH_2)_{1-3}$–SO_2– wherein any of the aryl or heteroaryl is optionally substituted by 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, phenyl, –O–C_{1-4}alkylphenyl, –S(O)–C_{1-4}alkyl, bromo, fluoro, chloro, or 2 substituents together form methylene dioxy; any (CH_2) optionally is substituted with C_{1-2}alkyl; or

B is



wherein the phenyl is optionally substituted by 1-3 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, bromo, fluoro, or chloro; and

X is H, OH, F, C_{1-4}alkyl, C_{1-4}alkoxy, –N(C_{0-5}alkyl)(C_{0-5}alkyl), phenyl, or =O.

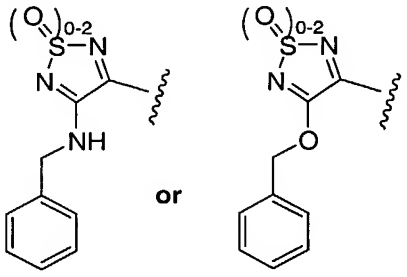
In an embodiment of the fourth aspect, the compounds of this invention are represented by Formula (I) or pharmaceutically acceptable salts thereof, wherein

NonAr is a nonaromatic 6 membered ring containing 1 nitrogen ring atom and 1 oxygen ring atom, wherein the remaining ring atoms are carbon;

A is a phenyl optionally substituted with 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-7}cycloalkyl, -CF_3, halogen, -OH, –CN, imidazolyl, -C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), -O-C_{1-4}alkyl, -C(O)-C_{0-4}alkyl, -C(O)-O-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkylphenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O-C_{1-4}alkyl, or –$NHSO_2$-C_{1-4}alkyl, -O-C_{1-4}alkylphenyl, or hydroxyiminoethyl; any alkyl optionally substituted with 1-6 –OH or halogen;

B is aryl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, heteroaryl$(CH_2)_{1-3}$–O–$(CH_2)_{0-2}$–C(O)–, indanyl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, aryl$(CH_2)_{1-3}$–C(O)–$(CH_2)_{0-2}$–, aryl–cyclopropyl–C(O)–$(CH_2)_{0-2}$–, heteroaryl$(CH_2)_{1-3}$–C(O)–, aryl$(CH_2)_{1-3}$–, heteroaryl$(CH_2)_{1-3}$–, aryl$(CH_2)_{1-3}$–NH–C(O)–, aryl$(CH_2)_{1-3}$–NH–C(NCN)–, aryl$(CH_2)_{1-3}$–SO_2–, aryl$(CH_2)_{0-3}$–S–$(CH_2)_{0-2}$–C(O)–, or heteroaryl$(CH_2)_{1-3}$–SO_2– wherein any of the aryl or heteroaryl is optionally substituted by 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, phenyl, –O–C_{1-4}alkylphenyl, –S(O)–C_{1-4}alkyl, bromo, fluoro, chloro, or 2 substituents together form methylene dioxy; any (CH_2) optionally is substituted with C_{1-2}alkyl; or

B is



wherein the phenyl is optionally substituted by 1-3 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, bromo, fluoro, or chloro; and

X is H, OH, F, C_{1-4}alkyl, C_{1-4}alkoxy, –N(C_{0-5}alkyl)(C_{0-5}alkyl), phenyl, or =O.

The term "cycloalkyl" means carbocycles containing no heteroatoms, and includes mono-, bi- and tricyclic saturated carbocycles, as well as fused ring systems. Such fused ring systems can include one ring that is partially or fully unsaturated such as a benzene ring to form fused ring systems such as benzofused carbocycles. Cycloalkyl includes such fused ring systems as spirofused ring systems. Examples of cycloalkyl include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, decahydronaphthalenyl, adamantanyl, indanyl, indenyl, fluorenyl, 1,2,3,4-tetrahydronaphthalenyl and the like. Similarly, "cycloalkenyl" means carbocycles containing no heteroatoms and at least one non-aromatic C-C double bond, and include mono-, bi- and tricyclic partially saturated carbocycles, as well as benzofused cycloalkenes. Examples of cycloalkenyl include cyclohexenyl, indenyl, and the like.

The term "cycloalkyloxy" unless specifically stated otherwise includes a cycloalkyl group connected to the oxy connecting atom.

The term "alkoxy" unless specifically stated otherwise includes an alkyl group connected to the oxy connecting atom.

The term "aryl" unless specifically stated otherwise includes multiple ring systems as well as single ring systems such as, for example, phenyl or naphthyl.

The term "aryloxy" unless specifically stated otherwise includes multiple ring systems as well as single ring systems such as, for example, phenyl or naphthyl, connected through the oxy connecting atom to the connecting site.

The term "C_0-C_6alkyl" includes alkyls containing 6, 5, 4, 3, 2, 1, or no carbon atoms. An alkyl with no carbon atoms is a hydrogen atom substituent when the alkyl is a terminus moiety. An alkyl with no carbon atoms is a direct bond when the alkyl is a bridging moiety.

The term "hetero" unless specifically stated otherwise includes one or more O, S, or N atoms. For example, heterocycloalkyl and heteroaryl include ring systems that contain one or more O, S, or N atoms in the ring, including mixtures of such atoms. The heteroatoms replace ring carbon atoms. Thus, for example, a heterocycloC_5alkyl is a five membered ring containing from 5 to no carbon atoms.

Examples of heteroaryl include, for example, pyridinyl, quinolinyl, isoquinolinyl, pyridazinyl, pyrimidinyl, pyrazinyl, quinoxalinyl, furyl, benzofuryl, dibenzofuryl, thienyl, benzothienyl, pyrrolyl, indolyl, pyrazolyl, indazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, imidazolyl, benzimidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl.

The term "heteroaryloxy" unless specifically stated otherwise describes a heteroaryl group connected through an oxy connecting atom to the connecting site.

Examples of heteroaryl(C_{1-6})alkyl include, for example, furylmethyl, furylethyl, thienylmethyl, thienylethyl, pyrazolylmethyl, oxazolylmethyl, oxazolylethyl, isoxazolylmethyl, thiazolylmethyl, thiazolylethyl, imidazolylmethyl, imidazolylethyl, benzimidazolylmethyl, oxadiazolylmethyl, oxadiazolylethyl, thiadiazolylmethyl, thiadiazolylethyl, triazolylmethyl, triazolylethyl, tetrazolylmethyl, tetrazolylethyl, pyridinylmethyl, pyridinylethyl, pyridazinylmethyl, pyrimidinylmethyl, pyrazinylmethyl, quinolinylmethyl, isoquinolinylmethyl and quinoxalinylmethyl.

Examples of heterocycloC$_{3-7}$alkyl include, for example, azetidinyl, pyrrolidinyl, piperidinyl, perhydroazepinyl, piperazinyl, morpholinyl, tetrahydrofuranyl, imidazolinyl, pyrolidin-2-one, piperidin-2-one, and thiomorpholinyl.

The term "*N*-heterocycloC4-7alkyl" describes nonaryl heterocyclic compounds having 3-6 carbon atoms and one nitrogen atom forming the ring. Examples include azetidinyl, pyrrolidinyl, piperidinyl, and perhydroazepinyl.

Examples of aryl(C_{1-6})alkyl include, for example, phenyl(C_{1-6})alkyl, and naphthyl(C_{1-6})alkyl.

Examples of heterocycloC$_{3-7}$alkylcarbonyl(C_{1-6})alkyl include, for example, azetidinyl carbonyl(C_{1-6})alkyl, pyrrolidinyl carbonyl(C_{1-6})alkyl, piperidinyl carbonyl(C_{1-6})alkyl, piperazinyl carbonyl(C_{1-6})alkyl, morpholinyl carbonyl(C_{1-6})alkyl, and thiomorpholinyl carbonyl(C_{1-6})alkyl.

The term "amine" unless specifically stated otherwise includes primary, secondary and tertiary amines.

Unless otherwise stated, the term "carbamoyl" is used to include -NHC(O)OC1-C4alkyl, and –OC(O)NHC1-C4alkyl.

The term "halogen" includes fluorine, chlorine, bromine and iodine atoms.

The term "optionally substituted" is intended to include both substituted and unsubstituted. Thus, for example, optionally substituted aryl could represent a pentafluorophenyl or a phenyl ring. Further, the substitution can be made at any of the groups. For example, substituted aryl(C_{1-6})alkyl includes substitution on the aryl group as well as substitution on the alkyl group.

The term "oxide" of heteroaryl groups is used in the ordinary well-known chemical sense and include, for example, *N*-oxides of nitrogen heteroatoms.

Compounds described herein may contain one or more asymmetric centers and may thus give rise to diastereomers and optical isomers. The present invention includes all such possible diastereomers as well as their racemic mixtures, their substantially pure resolved enantiomers, all possible geometric isomers, and pharmaceutically acceptable salts thereof. The above Formula I is shown without a definitive stereochemistry at certain positions. The present invention includes all stereoisomers of Formula I and pharmaceutically acceptable salts thereof. Further, mixtures of stereoisomers as well as isolated specific stereoisomers are also included. During the course of the synthetic procedures used to prepare such compounds, or in using racemization or epimerization procedures known to those skilled in the art, the products of such procedures can be a mixture of stereoisomers.

The term "pharmaceutically acceptable salts" refers to salts prepared from pharmaceutically acceptable non-toxic bases or acids. When the compound of the present invention is acidic, its corresponding salt can be conveniently prepared from pharmaceutically acceptable non-toxic bases, including inorganic bases and organic bases. Salts derived from such inorganic bases include aluminum, ammonium, calcium, copper (ic and ous), ferric, ferrous, lithium, magnesium, manganese (ic and ous), potassium, sodium, zinc and the like salts. Particularly preferred are the ammonium, calcium, magnesium, potassium and sodium salts. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines, as well as cyclic amines and substituted amines such as naturally occurring and synthesized substituted amines. Other pharmaceutically acceptable organic non-toxic bases from which salts can be formed include ion exchange resins such as, for example, arginine, betaine, caffeine, choline, N,N'-dibenzylethylenediamine, diethylamine, 2-diethylaminoethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, N-ethylmorpholine, N-ethylpiperidine, glucamine, glucosamine, histidine, hydrabamine, isopropylamine, lysine, methylglucamine, morpholine, piperazine, piperidine, polyamine resins, procaine, purines, theobromine, triethylamine, trimethylamine, tripropylamine, tromethamine and the like.

When the compound of the present invention is basic, its corresponding salt can be conveniently prepared from pharmaceutically acceptable non-toxic acids, including inorganic and organic acids. Such acids include, for

example, acetic, benzenesulfonic, benzoic, camphorsulfonic, citric, ethanesulfonic, fumaric, gluconic, glutamic, hydrobromic, hydrochloric, isethionic, lactic, maleic, malic, mandelic, methanesulfonic, mucic, nitric, pamoic, pantothenic, phosphoric, succinic, sulfuric, tartaric, p-toluenesulfonic acid and the like. Particularly preferred are citric, hydrobromic, hydrochloric, maleic, phosphoric, sulfuric, and tartaric acids.

The pharmaceutical compositions of the present invention comprise a compound represented by Formula I (or pharmaceutically acceptable salts thereof) as an active ingredient, a pharmaceutically acceptable carrier and optionally other therapeutic ingredients or adjuvants. The compositions include compositions suitable for oral, rectal, topical, and parenteral (including subcutaneous, intramuscular, and intravenous) administration, although the most suitable route in any given case will depend on the particular host, and nature and severity of the conditions for which the active ingredient is being administered. The pharmaceutical compositions may be conveniently presented in unit dosage form and prepared by any of the methods well known in the art of pharmacy.

In practice, the compounds represented by Formula I, or pharmaceutically acceptable salts thereof, of this invention can be combined as the active ingredient in intimate admixture with a pharmaceutical carrier according to conventional pharmaceutical compounding techniques. The carrier may take a wide variety of forms depending on the form of preparation desired for administration, e.g., oral or parenteral (including intravenous). Thus, the pharmaceutical compositions of the present invention can be presented as discrete units suitable for oral administration such as capsules, cachets or tablets each containing a predetermined amount of the active ingredient. Further, the compositions can be presented as a powder, as granules, as a solution, as a suspension in an aqueous liquid, as a non-aqueous liquid, as an oil-in-water emulsion or as a water-in-oil liquid emulsion. In addition to the common dosage forms set out above, the compound represented by Formula I, or pharmaceutically acceptable salts thereof, may also be administered by controlled release means and/or delivery devices. The compositions may be prepared by any of the methods of pharmacy. In general, such methods include a step of bringing into association the active ingredient with the carrier that constitutes one or more necessary ingredients. In general, the compositions are prepared by uniformly and intimately admixing the active ingredient with liquid carriers or finely divided solid carriers or both. The product can then be conveniently shaped into the desired presentation.

Thus, the pharmaceutical compositions of this invention may include a pharmaceutically acceptable carrier and a compound or a pharmaceutically acceptable salt of Formula I. The compounds of Formula I, or pharmaceutically acceptable salts thereof, can also be included in pharmaceutical compositions in combination with one or more other therapeutically active compounds.

The pharmaceutical carrier employed can be, for example, a solid, liquid, or gas. Examples of solid carriers include lactose, terra alba, sucrose, talc, gelatin, agar, pectin, acacia, magnesium stearate, and stearic acid. Examples of liquid carriers are sugar syrup, peanut oil, olive oil, and water. Examples of gaseous carriers include carbon dioxide and nitrogen.

In preparing the compositions for oral dosage form, any convenient pharmaceutical media may be employed. For example, water, glycols, oils, alcohols, flavoring agents, preservatives, coloring agents and the like may be used to form oral liquid preparations such as suspensions, elixirs and solutions; while carriers such as starches, sugars, microcrystalline cellulose, diluents, granulating agents, lubricants, binders, disintegrating agents, and the like may be used to form oral solid preparations such as powders, capsules and tablets. Because of their ease of administration, tablets and capsules are the preferred oral dosage units whereby solid pharmaceutical carriers are employed. Optionally, tablets may be coated by standard aqueous or nonaqueous techniques

A tablet containing the composition of this invention may be prepared by compression or molding, optionally with one or more accessory ingredients or adjuvants. Compressed tablets may be prepared by compressing, in a suitable machine, the active ingredient in a free-flowing form such as powder or granules, optionally mixed with a binder, lubricant, inert diluent, surface active or dispersing agent. Molded tablets may be made by molding in a suitable machine, a mixture of the powdered compound moistened with an inert liquid diluent. Each tablet preferably contains from about 1mg to about 500mg of the active ingredient and each cachet or capsule preferably containing from about 1 to about 500mg of the active ingredient.

Pharmaceutical compositions of the present invention suitable for parenteral administration may be prepared as solutions or suspensions of the active compounds in water. A suitable surfactant can be included such as, for example, hydroxypropylcellulose. Dispersions can also be prepared in glycerol, liquid

polyethylene glycols, and mixtures thereof in oils. Further, a preservative can be included to prevent the detrimental growth of microorganisms.

Pharmaceutical compositions of the present invention suitable for injectable use include sterile aqueous solutions or dispersions. Furthermore, the compositions can be in the form of sterile powders for the extemporaneous preparation of such sterile injectable solutions or dispersions. In all cases, the final injectable form must be sterile and must be effectively fluid for easy syringability. The pharmaceutical compositions must be stable under the conditions of manufacture and storage; thus, preferably should be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (e.g. glycerol, propylene glycol and liquid polyethylene glycol), vegetable oils, and suitable mixtures thereof.

Pharmaceutical compositions of the present invention can be in a form suitable for topical use such as, for example, an aerosol, cream, ointment, lotion, dusting powder, or the like. Further, the compositions can be in a form suitable for use in transdermal devices. These formulations may be prepared, utilizing a compound represented by Formula I of this invention, or pharmaceutically acceptable salts thereof, via conventional processing methods. As an example, a cream or ointment is prepared by mixing hydrophilic material and water, together with about 5 wt% to about 10 wt% of the compound, to produce a cream or ointment having a desired consistency.

Pharmaceutical compositions of this invention can be in a form suitable for rectal administration wherein the carrier is a solid. It is preferable that the mixture forms unit dose suppositories. Suitable carriers include cocoa butter and other materials commonly used in the art. The suppositories may be conveniently formed by first admixing the composition with the softened or melted carrier(s) followed by chilling and shaping in moulds.

In addition to the aforementioned carrier ingredients, the pharmaceutical formulations described above may include, as appropriate, one or more additional carrier ingredients such as diluents, buffers, flavoring agents, binders, surface-active agents, thickeners, lubricants, preservatives (including anti-oxidants) and the like. Furthermore, other adjuvants can be included to render the formulation isotonic with the blood of the intended recipient. Compositions containing a compound described by Formula I, or pharmaceutically acceptable salts thereof, may also be prepared in powder or liquid concentrate form.

Experimental Protocols

Assessing the Activity of Selected Compounds to Inhibit NR1A/2B NMDA Receptor Activation (FLIPR Assay)

The activity of selected compounds to inhibit NR1A/2B NMDA receptor activation measured as NR1A/2B receptor-mediated Ca^{2+} influx is assessed by the following procedure:

NR1A/2B receptor transfected L(tk) cells are plated in 96-well format at 3 x 10^6 cells per plate and grown for one - two days in normal growth media (Dulbeccos MEM with Na pyruvate, 4500mg glucose, pen/strep, glutamine, 10% FCS and 0.5mg/mL geneticin). NR1A/2B-expression in these cells is induced by the addition of 4nM dexamethasone in the presence of 500μM ketamine for 16 - 24 hours. After receptor induction cells are washed using a Labsystem Cellwasher two times with assay buffer (Hanks balanced salt solution (HBSS-Mg^{++} free) containing 20mM HEPES, 0.1% BSA, 2mM $CaCl_2$ and 250μM probenecid). The cells of each 96 well cell plate are loaded with the Ca^{++} sensitive dye Fluo-3 (Molecular Probes, Inc.) at 4μM in assay buffer containing 0.5% FBS, and 0.04% pluronic F-127 (Molecular Probes, Inc.) for 1h at 37 °C avoiding light. The cells are then washed with the Cellwasher four times with assay buffer leaving them in 100μL buffer. Test compounds in solution are pipetted by FLIPR (Fluorometric Imaging Plate Reader) into each test well for a 2min pretreatment. During this time the fluorescence intensity is recorded (excitation at 488nm and emission at 530nm). The glutamate/glycine 50μL agonist solution (final concentration 1μM/1μM) is then added by FLIPR into each well already containing 150μL of buffer (containing the test compound or vehicle) and the fluorescence is continuously monitored for 10min. The endpoint fluorescence values are used to determine an IC_{50} value comparing the agonist-stimulated signal for the vehicle alone sample and that for the cells incubated with each concentration of test compound.

Determining the Apparent Dissociation Constant (Ki) of Compounds for Human NR1A/NR2B Receptors (Binding Assay):

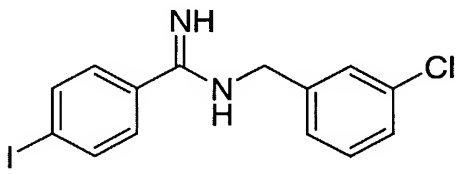
The radioligand binding assay is performed at room temperature in 96-well microtiter plates with a final assay volume of 1.0mL in 20mM HEPES buffer (pH 7.4) containing 150mM NaCl. Solutions of test compounds were prepared in DMSO and serially diluted with DMSO to yield 20μL of each of 10 solutions differing by 3-fold in concentration. Non-specific binding (NSB) using hot AMD-1 (10μM final concentration) and total binding (TB) by using DMSO (2% final concentration). A solution of NR1A/NR2B receptors (40pM final concentration) and tritiated AMD-2 (1nM final concentration) were added to the test compounds. After 3h of incubation at room temperature, samples are filtered through Packard GF/B filters (presoaked in 0.05% PEI, polyethyleninine Sigma P-3143) and washed 10 times with 1mL of cold 20mM HEPES buffer per wash. After vacuum drying of the filter plates, 40μL of Packard Microscint-20 was added and bound radioactivity determined in a Packard TopCount. The apparent dissociation constant (Ki), the maximum percentage inhibition ($\%I_{max}$), the minimum percentage inhibition ($\%I_{min}$) and the hill slope (nH) were determined by a non-linear least squares fitting the bound CPM data to Equation #1 below.

Equation #1:

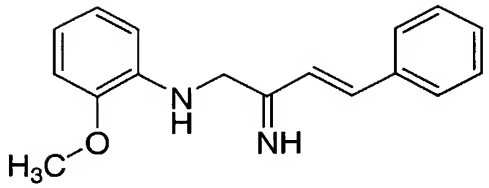
$$\text{CPM Bound} = \frac{(SB)\,(\%I_{max} - \%I_{min})}{(1 + ([Drug] / (Ki[AMD\text{-}2]/K_D))^{nH})} + NSB + (SB)\,(1 - \%I_{max})$$

where, K_D is the apparent dissociation constant for the radioligand for the receptor as determined by hot saturation and SB is the specifically bound CPM determined from the difference of TB and NSB.

AMD-1

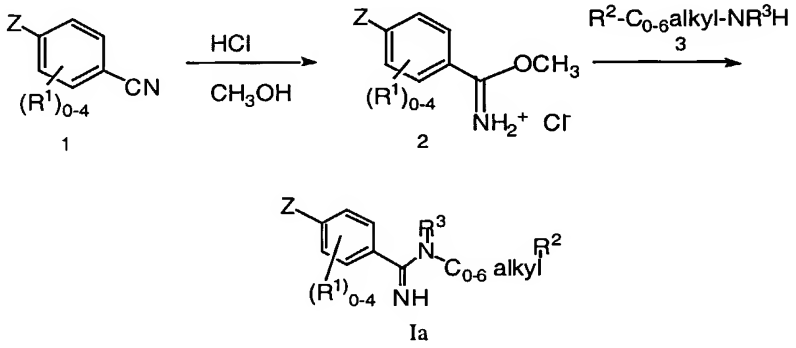


AMD-2



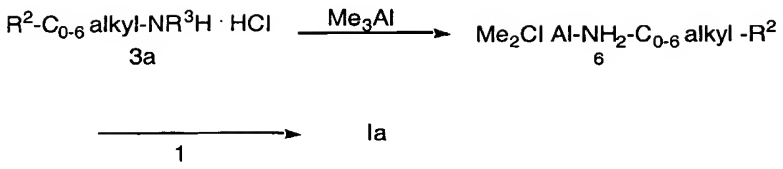
Compounds AMD-1 and AMD-2 can be synthesized in accordance with the following general reaction schemes.

SCHEME 1



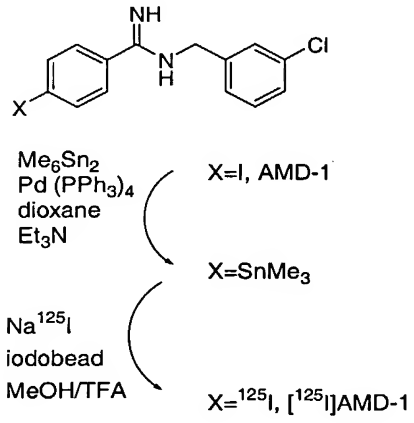
In accordance with scheme 1, hydrogen chloride is bubbled through a solution of the appropriately substituted benzonitrile 1 in methanol at room temperature. The volatiles are removed under reduced pressure and the resulting residue is triturated with ether and filtered to yield the desired imidate 2. Imidate 2 is dissolved in methanol at ambient temperature, treated with amine 3 at ambient temperature and stirred under argon. The volatiles are removed under reduced pressure and the residue purified by preparative HPLC or trituration with ether to afford amidine Ia.

SCHEME 2



In accordance with scheme 2, at room temperature under argon, amine 3a is dissolved in ether and was treated with 1-M hydrogen chloride in ether (1 equiv.) in a single portion. The resulting precipitate is stirred vigorously for 10 minutes. The volatiles are removed under reduced pressure. The residue is suspended in toluene, cooled to 0°C under argon, treated with 2.0-M trimethylaluminum (1.05 equiv.) in a dropwise manner, and stirred for 45 minutes at room temperature to afford intermediate 6 (not isolated). Compound 6 is added to a solution of nitrile 1 in toluene. The reaction is heated to 80°C without stirring in a sealed tube for 18h, cooled to ambient temperature, poured onto a silica gel column and eluted with methanol/dichloromethane to give the amidine 4.

Preparation of [^{125}I]AMD-1



Tritiated AMD-1 was prepared by the following procedure: A mixture of AMD-1, hydrochloride salt, (5mg, 0.012mmol) in dioxane (0.2mL) containing triethylamine (4μL) was treated with hexamethylditin (5μL), a catalytic amount of palladium catalyst and heated at 100°C for 45 minutes. The reaction was cooled to

room temperature, filtered through a glass wool plug, rinsed with methanol and concentrated *in vacuo* to give 10.7mg of a brown oil. The oil was dissolved in methylene chloride and passed through a small silica column eluting with methylene chloride followed by 5% methanol/methylene chloride. Fractions containing the trimethylstannane (Rf 0.26 in 10% methanol/methylene chloride) were pooled and concentrated *in vacuo* to give the trimethylstannane as a clear colorless oil. This material was further purified by HPLC (C18 Econosil, 10x250mm, 20 minute linear gradient, 30% MeCN:70% H_2O (0.1% TFA) to 90% MeCN, 3mL/min, 254nm, retention time 15 minutes) to give the trimethylstannane.

A $Na^{125}I$ shipping vial (10mCi, Amersham) was charged with a stir bar, an iodobead, 50μL of methanol and stirred five minutes at room temperature. A solution of the trimethylstannane (0.1mg) in 50μL of methanol containing 5μL of trifluoroacetic acid was added and the reaction was stirred for five minutes. The reaction was quenched with 50μL of ammonium hydroxide and purified by HPLC (C18 Vydac protein and peptide column, 4.6 x 250mm, 20 minute linear gradient, 30% MeCN:70% H_2O (0.1% TFA) to 90% MeCN, 1mL/min, retention time 11minutes). Fractions containing the radioactive product were pooled and concentrated *in vacuo* to give 989μCi of [^{125}I]AMD-1 with a specific activity of 898Ci/mmol as measured by UV absorbance at 272nm.

Synthesis of Tritiated AMD-2

Tritiated AMD-2 was prepared by the following procedure: The phenol of AMD-2 (2mg, 0.008mmol) dissolved in dimethylformamide (0.6mL) and potassium carbonate (1.2mg) for 1h. High specific activity tritiated methyl iodide (50mCi, 0.0006mmol, in toluene 1mL, American Radiolabeled Chemicals) was added at room temperature and stirred for 2 hours. The reaction mixture was filtered using a Whatman PTFE 0.45μm syringeless filter device to remove any insoluble potassium carbonate, washed with Abs. ethanol (2mL, Pharmco), and the combined filtrates were concentrated to dryness at room temperature using a rotary evaporator; this also removed any unreacted tritiated methyl iodide. The residue was purified by HPLC chromatography on a Phenomenx Luna C8 semi-prep column (Luna 5 micro C8(2), 250x10.0mm) using a gradient system of 20/80 acetonitrile/water with 0.1% trifluoroacetic acid to 100% acetonitrile with 0.1% trifluoroacetic acid in 20min.

Total activity of the product was 8mCi. Further purification was effected by absorption onto a Waters C-18 Sep-Pak column (Waters Sep-Pak PLUS C18) and elution with water followed by absolute ethanol. The product was diluted with absolute ethanol (10mL) before submission for final analysis.

The compounds of this invention exhibit IC_{50}'s of less than 50μM in the FLIPR and binding assays. Thus, the compounds and pharmaceutical compositions of this invention have been found to exhibit biological activity as NMDA NR2B antagonists. Advantageously, the IC_{50}'s should be less than 1μM in the FLIPR and binding assays. Even more advantageously, the IC_{50}'s should be less than 0.1μM in the FLIPR and binding assays. Accordingly, another aspect of the invention is the treatment of pain, migraine, depression, anxiety, schizophrenia, Parkinson's disease, or stroke – maladies that are amenable to amelioration through inhibition of NMDA NR2B receptors – by the administration of an effective amount of the compounds of this invention. Further, another aspect of the invention is the treatment of glaucoma and tinitis – maladies that are also amenable to amelioration through inhibition of NMDA NR2B receptors – by the administration of an effective amount of the compounds of this invention.

The abbreviations used herein are as follows unless specified otherwise:

BH_3*THF	Tetrahydrofuran/borane complex
BOC	t-Butoxycarbonyl
BOC_2O	t-Butoxycarbonyl anhydride
CBZ	Carbobenyloxy
CBZ-Cl	Carbobenzyl chloride
DCM	Dichloromethane
DIPEA	Diisopropylethylamine
DMF	N,N-Dimethylformamide
DMF-DMA	Dimethylformamide-Dimethylacetal
DMSO	Dimethylsulfoxide
EDC	3-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride
h	hours
HOAt	1-Hydroxy-7-azabenzotriazole

IPA	Isopropanol
*m*CPBA	meta Chloroperbenzoic acid
min	minutes
NMR	nuclear magnetic resonance
r.t. or rt	room temperature
sat.	saturated
TEA	Triethylamine
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran

The following examples are provided to more fully illustrate the present invention, and are not to be construed as limiting the scope of the claims in any manner.

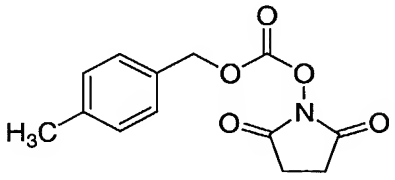
EXAMPLES

The compounds of this invention can be prepared by procedures shown below.

Intermediates:

INTERMEDIATE 1a:

Carbonic acid 2,5-dioxo-pyrrolidin-1-yl ester 4-methyl-benzyl ester



Disuccinimidyl carbonate (5.03g, 19.65mmol) in 30mL MeCN and 30mL DCM was treated with 4-methylbenzyl alcohol (2.4g, 19.6mmol) followed by DMAP (1.20g, 9.82mmol). The resulting cloudy reaction mixture was stirred overnight at rt, poured into 100mL water, and partitioned. The organic layer was dried over anhydrous sodium sulfate and the solvent evaporated. The solid thus

obtained was stirred with approx. 25mL ether, filtered, and the resulting product was washed with a small volume of ether and dried.

Ref: *Chem. Pharm. Bull.*, 38(1):110-115(1990).

The following compounds were similarly prepared in the manner described above for **INTERMEDIATE 1a**:

INTERMEDIATE 1b:

Carbonic acid 2,5-dioxo-pyrrolidin-1-yl ester 4-chloro-benzyl ester

INTERMEDIATE 1c:

Carbonic acid 2,5-dioxo-pyrrolidin-1-yl ester 4-fluoro-benzyl ester

INTERMEDIATE 1d:

Carbonic acid 2,5-dioxo-pyrrolidin-1-yl ester 4-ethyl-benzyl ester

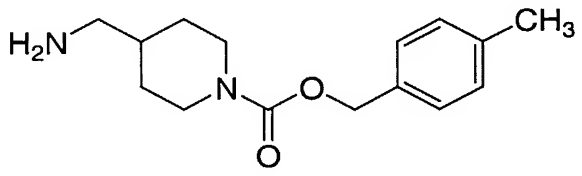
INTERMEDIATE 1e:

Carbonic acid 2,5-dioxo-pyrrolidin-1-yl ester 4-isopropyl-benzyl ester

Utilizing the carbonic acid derivatives described above as **INTERMEDIATES 1a-1e**, and following the procedure described below in **EXAMPLE 15, step 1**, the following **INTERMEDIATES 2a-2e** were obtained:

INTERMEDIATE 2a:

4-Methylbenzyl 4-(aminomethyl)piperidine-1-carboxylate



INTERMEDIATE 2b:

4-Chlorobenzyl 4-(aminomethyl)piperidine-1-carboxylate

INTERMEDIATE 2c:

4-Fluorobenzyl 4-(aminomethyl)piperidine-1-carboxylate

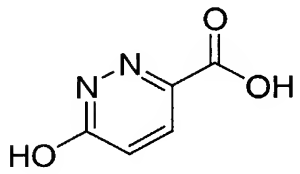
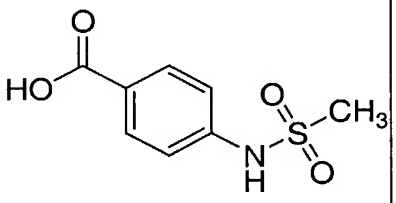
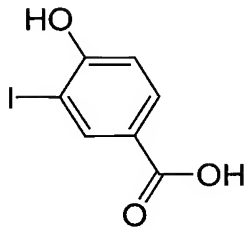
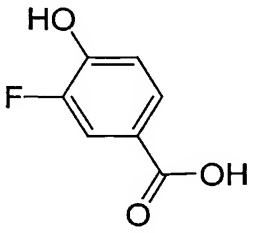
INTERMEDIATE 2d:

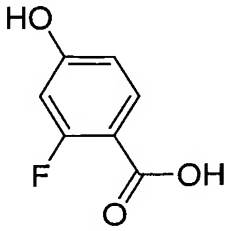
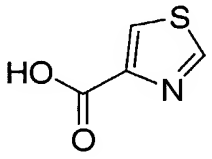
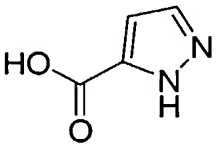
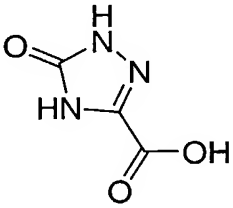
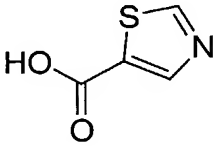
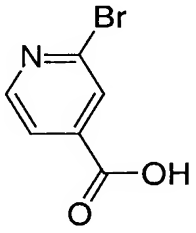
4-Ethylbenzyl 4-(aminomethyl)piperidine-1-carboxylate

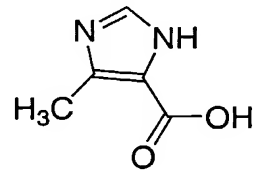
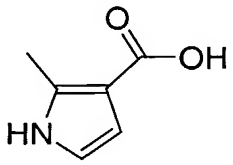
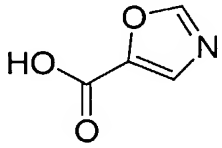
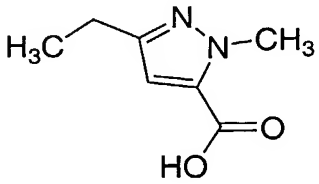
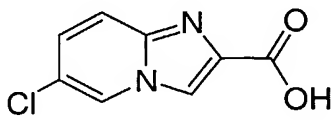
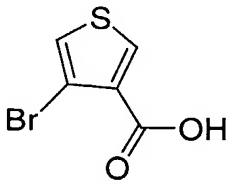
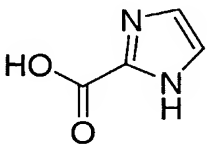
INTERMEDIATE 2e:

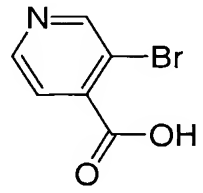
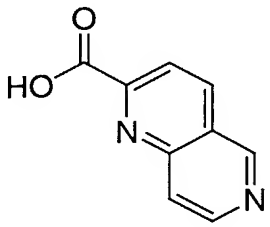
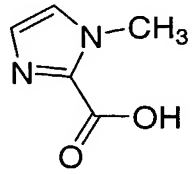
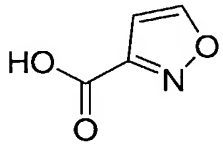
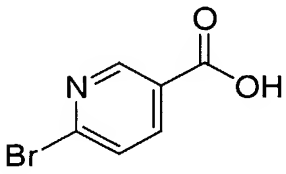
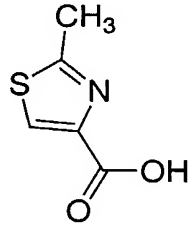
4-Isopropylbenzyl 4-(aminomethyl)piperidine-1-carboxylate

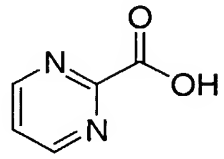
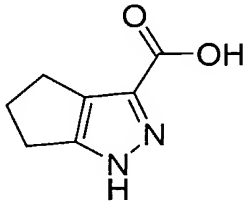
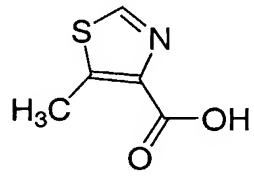
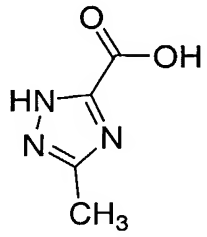
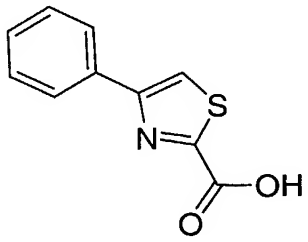
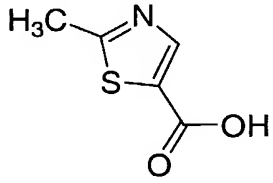
The carboxylic acids used in the coupling steps were either commercially available or prepared according to the following references:

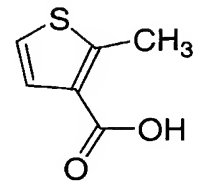
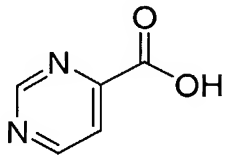
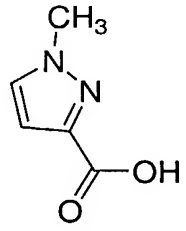
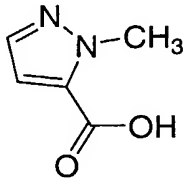
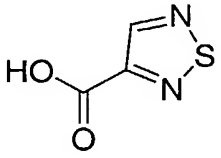
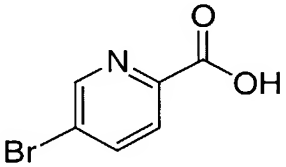
Structure	Name	Reference
	6-Hydroxy-pyridazine-3-carboxylic acid	M. Morishita, *Chem. Pharm. Bull.*, **42**:371(1994).
	4-Methanesulfonylamino-benzoic acid	L. Exner, *Collect Czech Chem. Comm*, 35:1371-1374(1970).
	4-Hydroxy-3-iodo-benzoic acid	L. C. King, et al., *J. Amer. Chem. Soc.*, 67:2089(1945).
	3-Fluoro-4-hydroxy-benzoic acid	J. Minor et al., *J. Org. Chem.*, (1952), **17**, 1425.

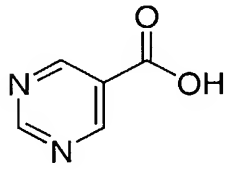
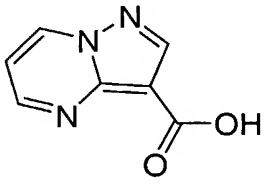
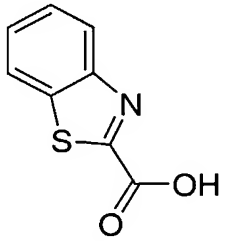
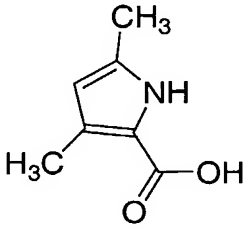
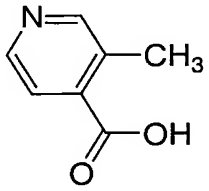
	2-Fluoro-4-hydroxy-benzoic acid	G. Gray et al., *Mol. Cryst. Liq. Cryst.*, 67:1-24(1981).
	Thiazole-4-carboxylic acid	H. Erlenmeyer et al., *Helv. Chim. Acta.*, 28:362(1945).
	2H-Pyrazole-3-carboxylic acid	Sokolov et al., *J. Gen. Chem. USSR* (Eng.) 52:2291(1982).
	5-Oxo-4,5-dihydro-1H-[1,2,4]triazole-3-carboxylic acid	Gehlen Ann (1952) **577**, 237-241.
	Thiazole-5-carboxylic acid	H. Erlenmeyer et al., *Helv. Chim. Acta.*, 30:1865(1947).
	2-Bromo-isonicotinic acid	A. Campbell et al., *Austral. J. Chem.*, 24:377(1971).

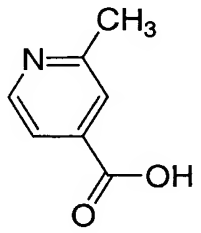
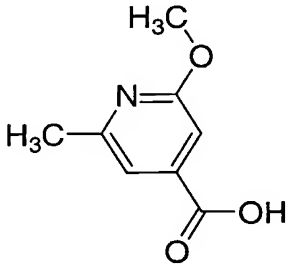
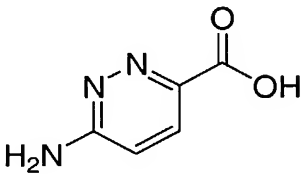
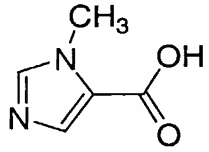
	5-Methyl-3H-imidazole-4-carboxylic acid	G. Wellman et al., *Synthesis* 356(1984).
	2-Methyl-1H-pyrrole-3-carboxylic acid	E. Benary, *Chemische Berichte*, 44:493(1911).
	Oxazole-5-carboxylic acid	U.S. Pat. No. 4,785,012
	5-Ethyl-2-methyl-2H-pyrazole-3-carboxylic acid	H. A. DeWald et al., *J. Med. Chem.*, 16:1346(1973).
	6-Chloro-imidazo[1,2-a]pyridine-2-carboxylic acid	WP 96/25414
	4-Bromo-thiophene-3-carboxylic acid	Tserng, K. et al., *J. Org. Chem.*, 40:172(1975).
	1H-Imidazole-2-carboxylic acid	Galeazzi, E. et al., *J. Org. Chem.*, 60:1090(1995).

	3-Bromo-isonicotinic acid	J. Dejardin et al., *Bull. Soc. Chim. Fr.*, 530(1976).
	[1,6]Naphthyridine-2-carboxylic acid	L. Chan et al., *J. Med. Chem.*, 42:3023(1999).
	1-Methyl-1H-imidazole-2-carboxylic acid	Shirley, D. A. et al., *J. Amer. Chem. Soc.*, 79:4922(1957).
	Isoxazole-3-carboxylic acid	R. Cramer et al., *J. Org. Chem.*, 26:2976(1961).
	6-Bromo-nicotinic acid	H. H. Bradlow et al., *J. Org. Chem.*, 14:509(1949).
	2-Methyl-thiazole-4-carboxylic acid	E. Jones et al., *J. Chem. Soc.*, 87(1946).

	Pyrimidine-2-carboxylic acid	A. Holland, *Chem. Ind.* (London), 786(1954).
	1,4,5,6-Tetrahydro-cyclopentapyrazole-3-carboxylic acid	N. Auwers, Justus Liebigs Annalen der Chemie, 536:97-109(1938).
	5-Methyl-thiazole-4-carboxylic acid	G. D. Hartman et al., *Synthesis*, 681(1976).
	5-Methyl-2H-[1,2,4]triazole-3-carboxylic acid	J. Dost, *Z. Chem.*, 26:203(1986).
	4-Phenyl-thiazole-2-carboxylic acid	R. Canas et al., Ann. Rev. Soc. Esp. Fis. Quim., 50:609-614(1954).
	2-Methyl-thiazole-5-carboxylic acid	A. Schöberl et al., Ber, 73:1240(1940).

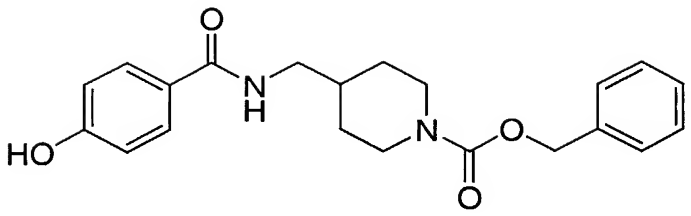
	2-Methyl-thiophene-3-carboxylic acid	E. Bullock et al., *Can. J. Chem.*, 55:895(1977).
	Pyrimidine-4-carboxylic acid	G. A. Archer et al., *J. Med. Chem.* 16:1312(1977).
	1-Methyl-1H-pyrazole-3-carboxylic acid	C. Wijnberger et al., *J. Heterocycl. Chem.*, 6:545(1969).
	2-Methyl-2H-pyrazole-3-carboxylic acid	C. Wijnberger et al., *J. Heterocycl. Chem.*, 6:545(1969).
	[1,2,5]Thiadiazole-3-carboxylic acid	L. M. Weinstock et al., *Adv. Heterocycl. Chem.*, 9:107(1968).
	5-Bromo-pyridine-2-carboxylic acid	L. W. Deady et al., *Austral. J. Chem.*, 24:385(1971).

	Pyrimidine-5-carboxylic acid	H. Bredereck et al., *Liebigs Ann. Chem,*. (1972), **766**, 73(1972).
	Pyrazolo[1,5-a]pyrimidine-3-carboxylic acid	Khan et al., *J. Heterocycl. Chem.*, **7**:247(1970).
	Benzothiazole-2-carboxylic acid	A. Buraway et al., *J. Chem. Soc.*, 648(1956).
	3,5-Dimethyl-1H-pyrrole-2-carboxylic acid	H. Fischer et al., *Chemische Berichte*, 56:1194(1923).
	3-Methyl-isonicotinic acid	R.S. Miu et al., *Chem. Abstract.*, 84:150463(1976).

	2-Methyl-isonicotinic acid	R. Adams et al., *J. Amer. Chem. Soc.*, 76:3168(1954).
	2-Methoxy-6-methyl-isonicotinic acid	WO 00/17163
	6-Amino-pyridazine-3-carboxylic acid	S. Mitsui, *Chem. Abstract.*, 5275(1959).
	3-methyl-3H-imidazole-4-carboxylic acid	EP 0306868

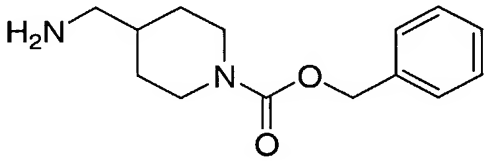
EXAMPLE 1:

4-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester



Step 1:

Preparation of Benzyl 4-(aminomethyl)piperidine-1-carboxylate

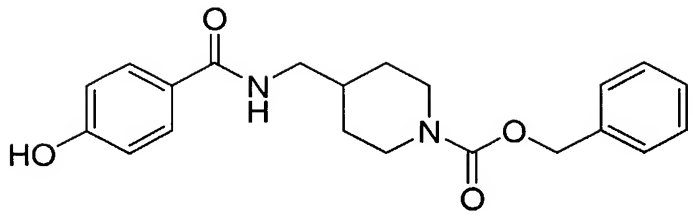


4-Aminomethylpiperidine (40g, 350mmol) and benzaldehyde (37.3mL, 368mmol) in toluene (600mL) were heated to reflux under dean stark conditions for 2h. The resulting reaction mixture was cooled to room temperature and 500mL dichloromethane was added. The resulting solution was cooled to 5°C and treated with N-(benzyloxycarbonyloxy)succinimide (91.7g, 368mmol). After 10min, the cooling bath was removed and the reaction mixture stirred for 1h. The solvents were evaporated and the resulting residue was stirred with 400mL THF and 400mL 2M HCl for 1h. The mixture was concentrated to remove organics and was then extracted with ether (3x300mL). The aqueous phase was adjusted to pH14 with 50% NaOH and extracted with ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous sodium sulfate, and the solvent evaporated to give benzyl 4-(aminomethyl)piperidine-1-carboxylate as an oil.

^{1}H NMR 500MHz (δ, $CDCl_3$) δ: 7.4-7.2 (m, 5H); 5.12 (s, 2H); 4.20 (brs, 2H); 2.77 (brs, 2H); 2.58 (d, J=6.6 Hz, 2H) 1.9-1.7 (m, 2H); 1.0-1.5 (m, 5H).

Step 2:

Preparation of 4-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester



To a mixture of 4-hydroxybenzoic acid (2.5g, 0.0182mol), 1-hydroxybenzotriazole hydrate (3.33g, 0.0218mol), benzyl 4-(aminomethyl)piperidine-1-carboxylate (4.5g, 0.0182mol) and triethylamine (3.03mL, 0.0218mol) in DMF (30mL) was added 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (4.2g, 0.0218mol) and the mixture allowed to stir at rt for 18h. The mixture was quenched into water (200mL) and extracted with ethyl acetate (200mL). The ethyl acetate extract was washed with 10% aqueous sodium bicarbonate (100mL), brine (50mL), dried over sodium sulfate, and filtered. The filtrate was concentrated in vacuo and the residue chromatographed on silica using 10-20% acetone/dichloromethane to give 6.3g of 4-[(4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester as a foam. The foam was dissolved in hot isopropyl acetate (125mL), filtered, and allowed to cool and crystallize. The reaction volume was reduced in vacuo to 50mL, allowed to stir overnight at rt and filtered. The resulting solid was dried in vacuo (50°C) yielding the 4-[(4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester.

M.P. 122-123°C. M.S(M+1): 369.

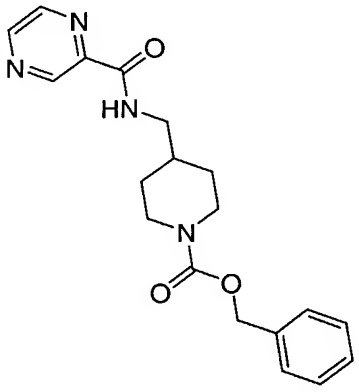
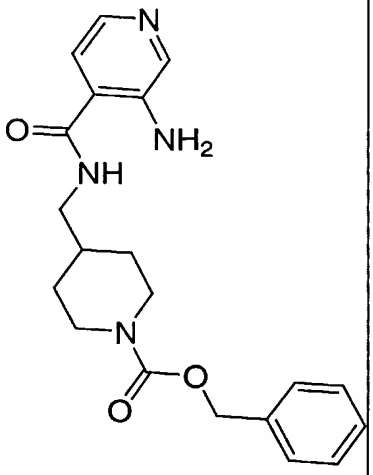
^{1}H NMR 300MHz (δ, $CDCl_3$) δ: 7.64 (d, 2H); 7.4-7.2 (m, 5H); 6.86 (d, 2H); 6.18(m, 1H); 5.85(s, 1H); 5.15 (s, 2H); 4.20 (brs, 2H); 3.35 (brs, 2H); 2.77 (brs, 2H); 1.9-1.7 (m, 3H); 1.3-1.1 (m, 2H).

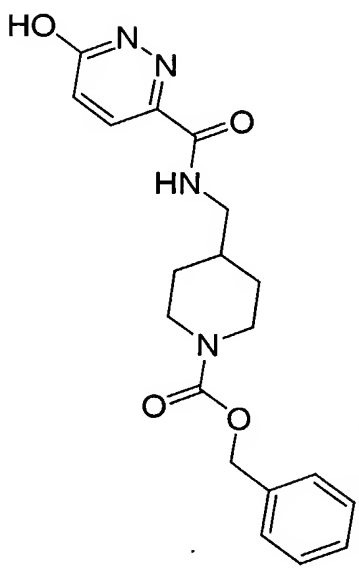
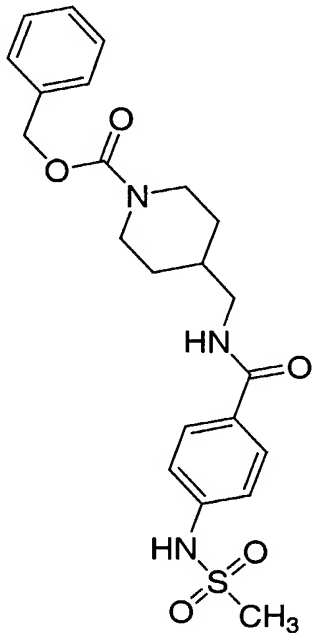
Analysis Calcd. for $C_{21}H_{24}N_2O4$: C, 68.46; H, 6.57; N, 7.60;

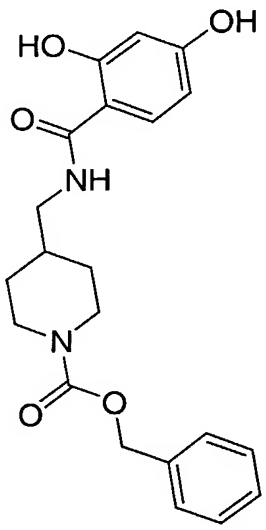
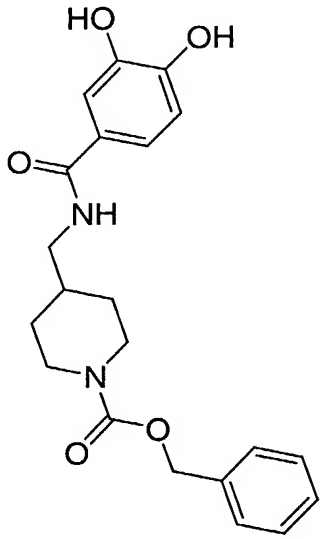
Found: C, 68.23; H, 6.61; N, 7.48.

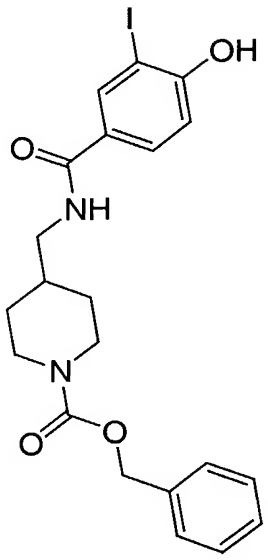
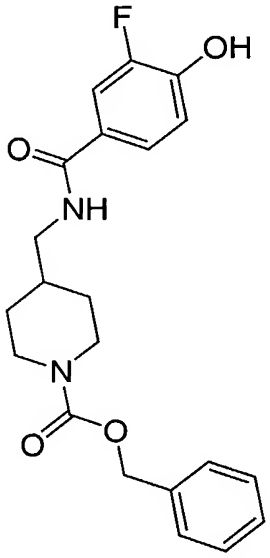
The following compounds were prepared in a manner similar to that used above for the preparation of 4-[(4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester, using the appropriate acid in place of the 4-hydroxybenzoic acid. References or experimental procedures are shown for the preparation of non-commercially available acids. Appropriately substituted benzyl 4-(aminomethyl)piperidine-1-carboxylates were prepared in a similar manner to that described above in **EXAMPLE 1**, step 1, with the necessary

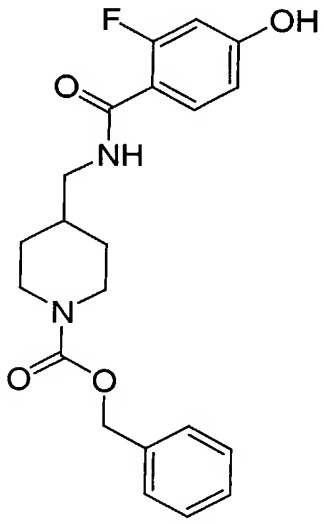
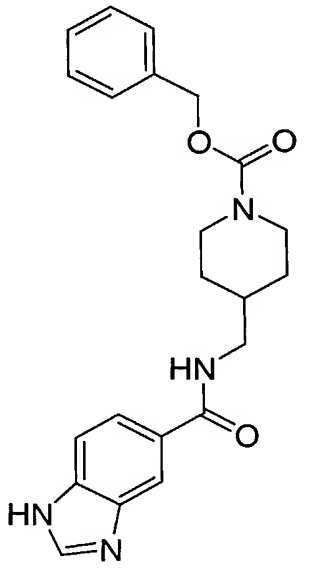
N-(benzyloxycarbonyloxy)succinimides prepared as previously described (Chem. Pharm Bull 1990, 38(1) 110-115).

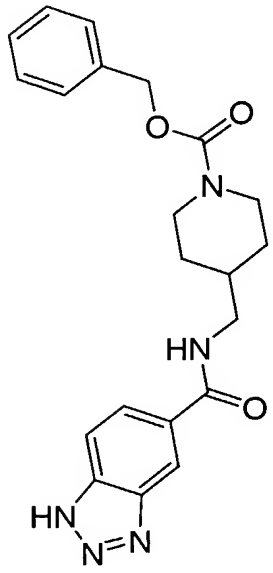
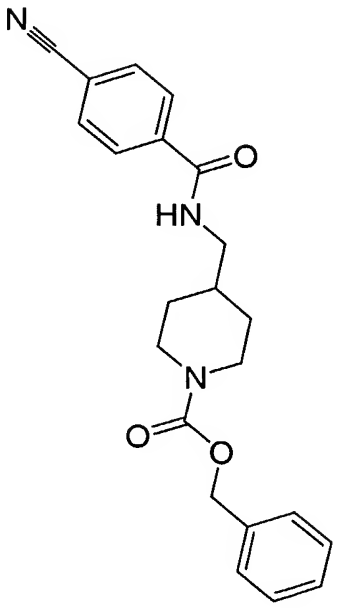
EX.	Name	Structure	Data
2.	**4-{[(Pyrazine-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S(M+1): 370 ^{1}H NMR 300MHz (δ, $CDCl_3$) δ: 12.10 (brs, 1H); 8.02 (d, 1H, J=2.5 Hz); 7.77 (dd, 1H, J=7.7 and 2.5Hz); 7.4-7.2 (m, 5H); 6.59 (d, 2H, J=7.7 Hz); 6.12 (m, 1H); 5.12 (s, 2H); 4.20 (brs, 2H); 3.30 (brs, 2H); 2.77 (brs, 2H); 2.0-1.8 (m, 3H); 1.3-1.1 (m, 2H).
3.	**4-{[(3-Amino-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S(M+1): 369 NMR (300MHz, $CDCl_3$) δ: all broad

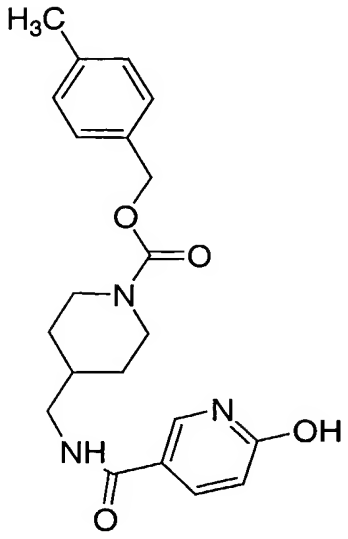
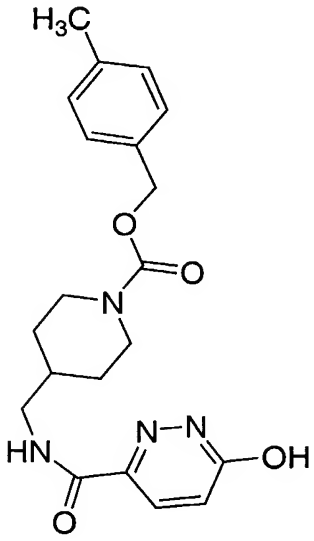
EX.	Name	Structure	Data
4.	**4-{[(6-Hydroxy-pyridazine-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S(M+1): 371 NMR (300MHz, $CDCl_3$) δ: 11.55 (brs, 1H); 8.04 (d, 1H, J=9.8 Hz); 7.4-7.1 (m, 5 H); 7.04 (d, 1H, 9.8Hz); 5.12(s, 2H); 4.22(brs, 2H); 3.30 (brs, 2H); 2.80(m, 2H); 1.8-1.6 (m, 3H); 1.3-1.1 (m, 2H)
5.	**4-[(4-Methanesulfonylamino-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester**		M.S(M+1): 446NMR (300MHz, $CDCl_3$)) δ: 7.75 (d, 2H, J=8.6 Hz); 7.4-7.2 (m, 5H); 7.25 (d, 2H, J=8.6 Hz); 6.95 (brs, 1H); 6.25 (brs, 1H); 5.12 (s, 2H); 4.21 (brs, 2H); 4.36 (brs, 2H); 3.05 (s, 3H); 2.78 (brs, 2H); 1.9-1.6 (m, 3H); 1.3-1.1 (m, 2H).

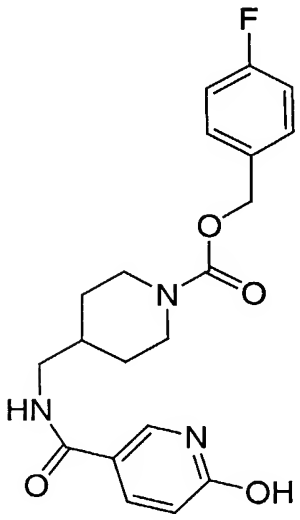
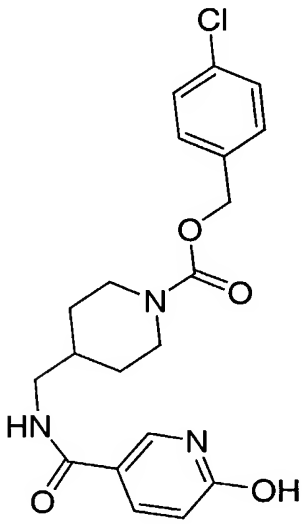
EX.	Name	Structure	Data
6.	**4-[(2,4-Dihydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester**		M.S(M+1): 385NMR (300MHz, $CDCl_3$)) δ: 12.55(s, 1H); 7.5-7.3(m, 5H); 7.22 (d, 1H, J=8.6 Hz); 6.41 (d, 1H, J=2.5 Hz); 6.34 (dd, 1H, J=8.6 and 2.5 Hz); 6.22 (m, 1H); 5.13 (s, 2H); 4.22 (brs, 2H); 3.33 (brs, 2H); 2.79 (brs, 2H); 1.8-1.6 (m, 3H); 1.3-1.0 (m, 2H).
7.	**4-[(3,4-Dihydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester**		M.S(M+1): 385NMR (300MHz, $CDCl_3$)) δ: 7.57(d, 1H, J=1.6 Hz); 7.5-7.3(m, 5H); 7.10 (dd, 1H, J=8.2 and 1.6 Hz); 6.86 (d, 1H, J=8.2 Hz); 6.30 (m, 1H); 5.12 (s, 2H); 4.18 (brs, 2H); 3.32 (brs, 2H); 2.76 (brs, 2H); 1.8-1.4 (m, 3H); 1.3-1.0 (m, 2H).

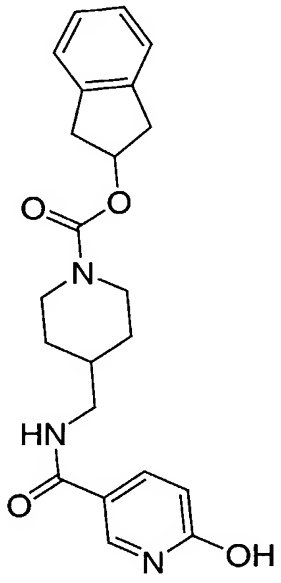
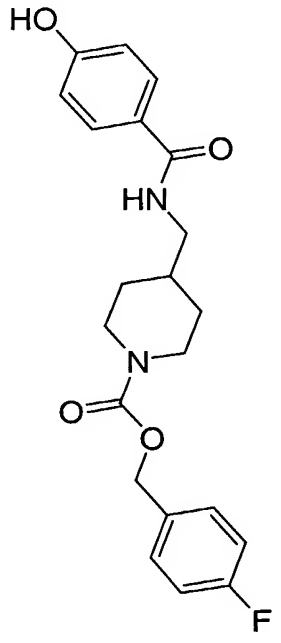
EX.	Name	Structure	Data
8.	**4-[(4-Hydroxy-3-iodo-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester**		M.S(M+1): 495 NMR (300MHz, $CDCl_3$)) δ: 8.11(d, 1H, J=2.1 Hz); 7.63(dd, 1H, J=8.4 and 2.1 Hz); 7.5-7.3(m, 5H); 7.00 (d, 1H, J=8.4 Hz); 6.10 (m, 1H); 5.12 (s, 2H); 4.21 (brs, 2H); 3.33 (brs, 2H); 2.78 (brs, 2H); 1.8-1.6 (m, 3H); 1.3-1.0 (m, 2H).
9.	**4-[(3-Fluoro-4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester**		M.S(M+1): 387 NMR (300MHz, $CDCl_3$)) δ: 7.56(dd, 1H, J=11.0 and 1.9 Hz); 7.5-7.3(m, 6H); 7.03 (t, 1H, J=8.4 Hz); 6.16 (m, 1H); 5.12 (s, 2H); 4.20 (brs, 2H); 3.33 (brs, 2H); 2.78 (brs, 2H); 1.9-1.6 (m, 3H); 1.3-1.0 (m, 2H).

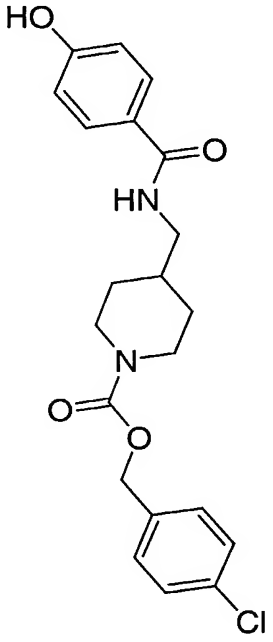
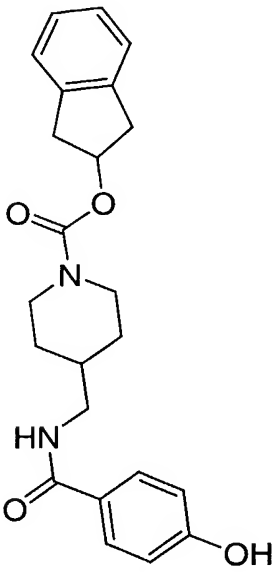
EX.	Name	Structure	Data
10.	**4-[(2-Fluoro-4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester**		M.S(M+1): 387 NMR (300MHz, $CDCl_3$)) δ:7.94 (t, 1H, J=9.0 Hz); 7.5-7.2 (m, 5H); 6.78 (m, 1H); 7.73(dd, 1H, J=8.7 and 2.4 Hz); 6.61(dd, 1H, J=13.8 and 2.2 Hz); 5.13 (s, 2H); 4.20 (brs, 2H); 3.37 (brs, 2H); 2.78 (brs, 2H); 1.9-1.6 (m, 3H); 1.3-1.0 (m, 2H).
11.	**4-{[(1H-Benzoimidazole-5-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		MS Exact mass: 393.1940. Experimental for $C_{21}H_{24}N_4O_3$: 393.1921. ^1H NMR (400MHz, δ, $CDCl_3$): 8.13-8.11 (m, 2H), 7.67 (brs, 2H), 7.35-7.28 (m, 5H), 6.52 (d, J=5.98Hz, 2H), 5.13 (s, 2H), 4.21 (brs,2H), 3.39 (brs, 2H), 2.79 (brs, 2H), 1.90-1.78 (m, 1H), 1.78-1.62 (m, 2H), 1.29-1.16 (m, 2H).

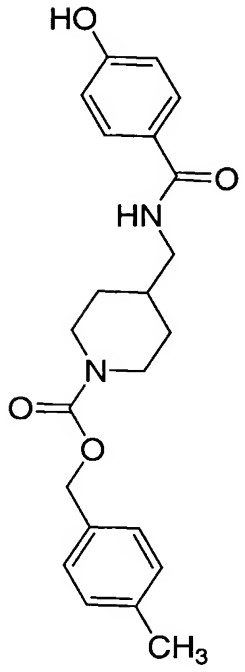
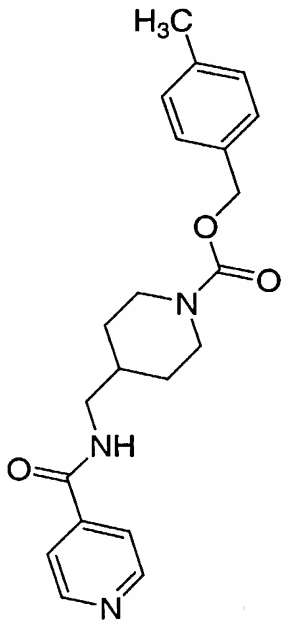
EX.	Name	Structure	Data
12.	**4-{[(1H-Benzotriazole-5-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		MS Exact mass: 394.1896. Experimental for $C_{21}H_{23}N_5O_3$: 394.1874. ^{1}H NMR (400MHz, δ, $CDCl_3$): 8.37 (s, 1H), 7.78 (d, J=8.68Hz, 2H), 7.66-7.64 (m, 2H), 7.31-7.22 (m, 5H), 6.65 (vbs, 2H), 5.09 (s, 2H), 4.13 (brd, J=11.06, 2H), 3.35 (brs, 2H), 2.71 (brs, 2H), 1.90-1.77 (m, 1H), 1.71 (brd, J=11.61Hz, 2H), 1.26-1.12 (m, 2H).
13.	**4-[(4-Cyano-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.86 (d, J=8.05 Hz, 2H), 7.74 (d, J=8.05Hz, 2H), 7.25-7.4 (m, 5H), 6.31 (brt, J= 5.61 Hz, 1H), 5.12 (s,2H), 4.22 (brs, 2H), 3.37 (brs, 2H), 2.79 (brs, 2H), 1.7-1.9 (m, 3H), 1.23 (m, 2H).

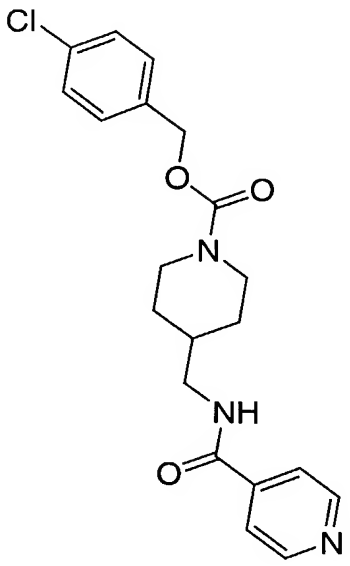
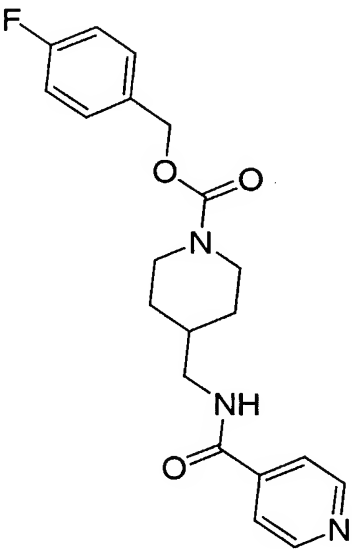
EX.	Name	Structure	Data
14.	**4-{[(6-Hydroxy-pyridine-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester**		M.S(M+1): 384 NMR (300MHz, $CDCl_3$) δ: 12.20 (brs, 1H); 8.02 (d, 1H, J=2.5 Hz); 7.75 (dd, 1H, J=9.6 and 2.5 Hz); 7.24 (d, 2H, J= 7.9Hz); 7.15 (d, 2H, J=7.9 Hz); 6.56 (d, 1H, J=9.6Hz); 6.20 (m, 1H); 5.07 (s, 2H); 4.20 (brs, 2H); 3.30 (brs, 2H); 2.35 (brs, 2H); 1.8-1.6 (m, 3H); 1.3-1.1 (m, 2H).
15.	**4-{[(6-Hydroxy-pyridazine-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester**		M.S(M+1): 385 NMR (300MHz, $CDCl_3$)) δ: 11.9 (s, 1H); 8.05 (d, 1H, J=9.9 Hz); 7.25 (d, 2H, J=7.9 Hz); 7.16 (d, 2H, J=7.9 Hz); 7.04 (d, 1H, J=9.9 Hz); 5.08 (s, 2H); 4.20 (brs, 2H); 3.32 (brs, 2H); 2.76 (m, 2H);2.35 (s, 3H); 1.8-1.6 (m, 3H); 1.3-1.1 (m, 2H).

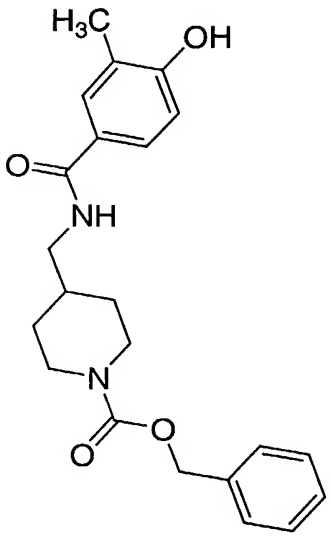
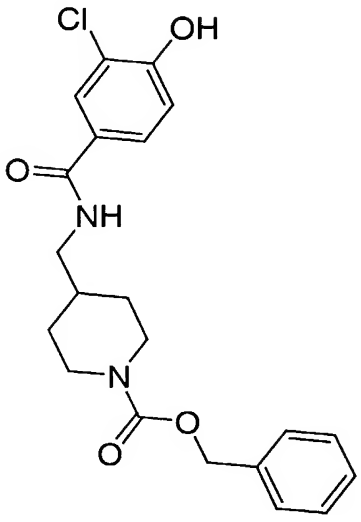
EX.	Name	Structure	Data
16.	**4-{[(6-Hydroxy-pyridine-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-fluoro-benzyl ester**		M.S(M+1): 388 NMR (300MHz, $CDCl_3$)) δ: 12.2 (s, 1H); 8.03 (d, 1H, J=2.6 Hz); 7.77 (dd, 1H, J=9.6 and 2.6 Hz); 7.34 (m, 2H); 7.03 (t, 2H, J=8.6 Hz); 6.57 (d, 1H, J=9.6 Hz); 5.07 (s, 2H); 4.20 (brs, 2H); 3.31 (brs, 2H); 2.76 (brs, 2H);2.35 (s, 3H); 1.8-1.6 (m, 3H); 1.3-1.1 (m, 2H).
17.	**4-{[(6-Hydroxy-pyridine-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-chloro-benzyl ester**		M.S(M+1): 404 NMR (300MHz, $CDCl_3$)) δ: 11.8 (brs, 1H); 8.02 (d, 1H, J=2.4 Hz); 7.74 (dd, 1H, J=9.6 and 2.4 Hz); 7.4-7.2 (m, 4H); 6.58 (d, 1H, J=9.6 Hz); 6.03 (m, 1H); 5.08 (s, 2H); 4.20 (brs, 2H); 3.31 (brs, 2H); 2.78 (brs, 2H); 1.8-1.4 (m, 3H); 1.3-1.1 (m, 2H).

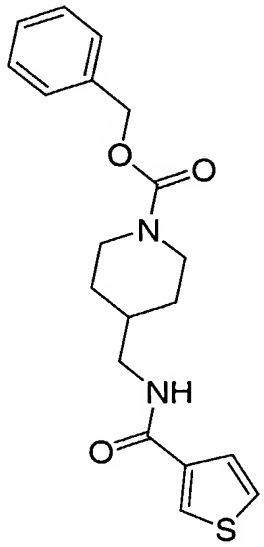
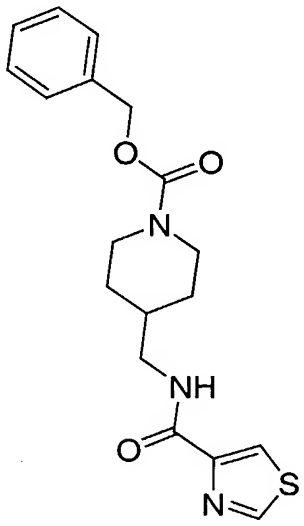
EX.	Name	Structure	Data
18.	**4-{[(6-Hydroxy-pyridine-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid indan-2-yl ester**		M.S(M+1): 396 NMR (300MHz, $CDCl_3$)) δ: 12.0 (brs, 1H); 8.01 (d, 1H, J=2.5 Hz); 7.74 (dd, 1H, J=9.6 and 2.5 Hz); 7.3-7.1 (m, 4H); 6.57 (d, 1H, J=9.6 Hz); 6.04 (m, 1H); 5.46 (m, 1H); 4.3-4.1 (m, 2H); 3.32 (m, 4H); 3.04 (d, 1H, J=3.2 Hz); 3.00 (d, 1H, J=3.2 Hz); 2.72 (m, 2H); 1.8-1.6 (m, 3H); 1.3-1.0 (m, 2H).
19.	**4-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid 4-fluoro-benzyl ester**		M.S(M+1): 387NMR (300MHz, $CDCl_3$)) δ: 7.65 (d, 2H, J=8.6 Hz); 7.33 (m, 2H); 7.03 (t, 2H, J=8.6 Hz); 6.86 (d, 2H, J=8.6 Hz); 6.64 (s, 1H); 6.22 (m, 1H); 5.08(s, 2H); 4.14 (brs, 2H); 3.33 (brs, 2H); 2.67 (brs, 2H); 1.8-1.6 (m, 3H); 1.3-1.0 (m, 2H).

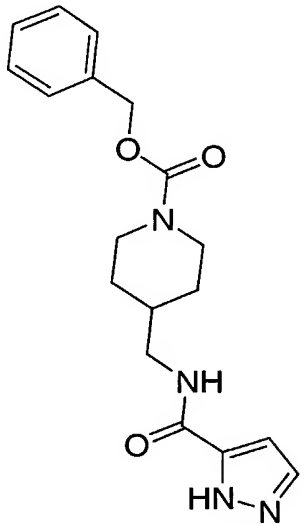
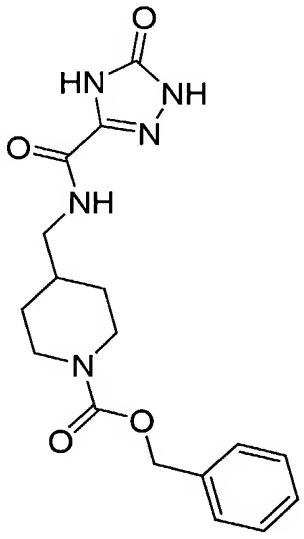
EX.	Name	Structure	Data
20.	**4-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid 4-chloro-benzyl ester**		M.S(M+1): 403 NMR (300MHz, $CDCl_3$)) δ: 7.66 (d, 2H, J=8.6 Hz); 7.30 (m, 4H); 6.86 (d, 2H, J=8.6 Hz); 6.33 (s, 1H); 6.22 (m, 1H); 5.08(s, 2H); 4.14 (brs, 2H); 3.33 (brs, 2H); 2.77 (brs, 2H); 1.8-1.6 (m, 3H); 1.3-1.0 (m, 2H).
21.	**4-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid indan-2-yl ester**		M.S(M+1): 395NMR (300MHz, $CDCl_3$)) δ: 7.63 (d, 2H, J=8.6 Hz); 7.3-7.1 (m, 4H); 6.85 (d, 2H, J=8.6 Hz); 6.27 (m, 1H); 5.46 (m, 1H); 4.3-3.8 (m, 2H); 3.3 (dd, 4H, J=16.9 and 6.6 Hz); 3.0 (dd, 2H, J=7.0 and 3.2 Hz); 2.69 (dt, 2H, J=13.2 and 2.7 Hz); 1.8-1.6 (m, 3H); 1.3-1.0 (m, 2H).

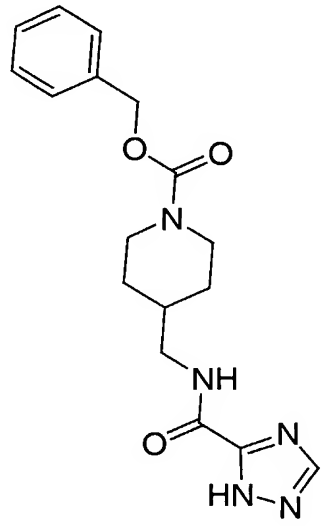
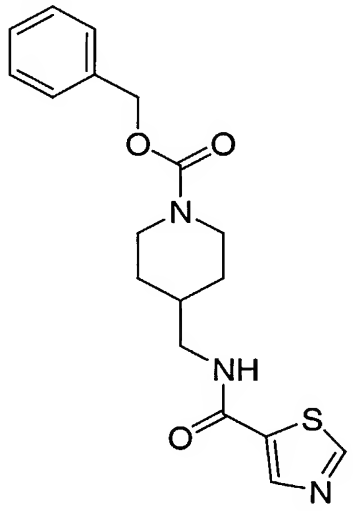
EX.	Name	Structure	Data
22.	**4-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid 4-methyl-benzyl ester**		M.S(M+1): 383 NMR (300MHz, $CDCl_3$)) δ: 7.64 (d, 2H, J=8.8 Hz); 7.24 (d, 1H, J=8.0 Hz); 7.15(d, 1H, J=8.0 Hz); 6.86 (d, 2H, J=8.8 Hz); 6.24 (m, 1H); 5.08 (s, 2H); 4.18 (brs, 2H); 3.32 (brs, 2H); 2.75 (brs, 2H); 2.34 (s, 3H); 1.8-1.6 (m, 3H); 1.3-1.0 (m, 2H).
23.	**4-{[(Pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester**		^1H NMR (δ, $CDCl_3$): 8.75 (d, J=5.86Hz, 2H), 7.60 (d, J=4.89 Hz, 2H), 7.25 (d, J=8.05 Hz, 2H), 7.16 (d, J=8.05Hz, 2H), 6.32 (brt, 1H), 5.08 (s,2H), 4.22 (brs, 2H), 3.37 (brs, 2H), 2.77 (brs, 2H), 2.35 (s, 3H), 1.7-1.9 (m, 3H), 1.21 (m, 2H).

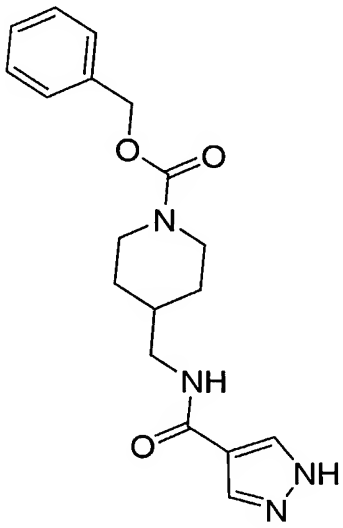
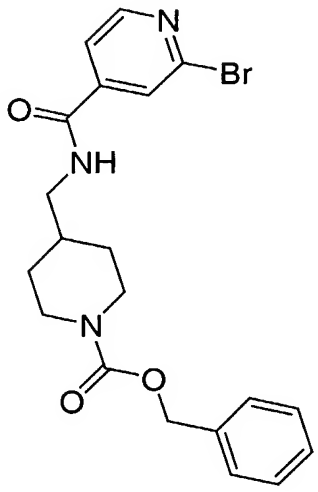
EX.	Name	Structure	Data
24.	**4-{[(Pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-chloro-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 8.75 (d, J=4.64 Hz, 2H), 7.60 (d, J=5.13 Hz, 2H), 7.32 (d, J=8.05 Hz, 2H), 7.28 (d, J=8.55 Hz, 2H), 6.35 (brt, 1H), 5.08 (s,2H), 4.22 (brd, 2H), 3.37 (brd, 2H), 2.79 (brs, 2H), 1.7-1.9 (m, 3H), 1.23 (m, 2H).
25.	**4-{[(Pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-fluoro-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 8.75 (d, J=5.61 Hz, 2H), 7.60 (d, J=6.11 Hz, 2H), 7.28 (dd, J=5.62, 8.3 Hz, 2H), 7.04 (t, J=8.8 Hz, 2H), 6.33 (brt, 1H), 5.08 (s,2H), 4.23 (brd, 2H), 3.38 (brd, 2H), 2.78 (brs, 2H), 1.7-1.9 (m, 3H), 1.22 (m, 2H).

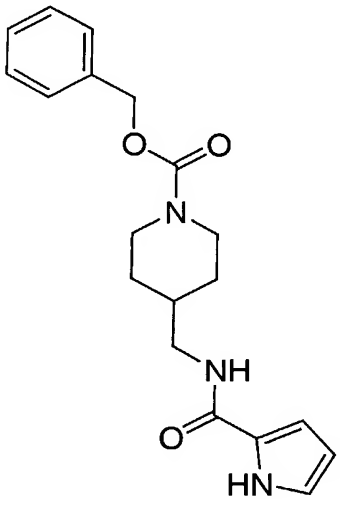
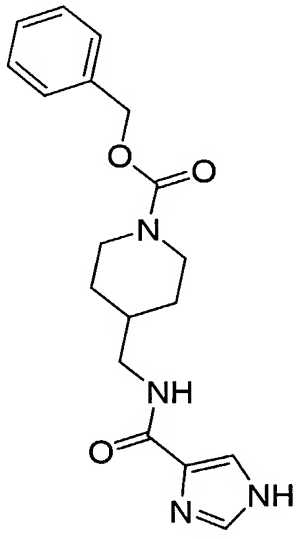
EX.	Name	Structure	Data
26.	**4-[(4-Hydroxy-3-methyl-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.56 (brs, 1H), 7.49 (dd, J=2.2, 8.3 Hz, 1H), 7.25-7.4 (m, 5H), 6.79 (d, J=8.3 Hz, 1H), 6.13 (brt, 1H), 5.55 (s,1H), 5.12 (s,2H), 4.22 (brs, 2H), 3.33 (brs, 2H), 2.78 (brs, 2H), 2.28 (s,3H), 1.7-1.9 (m, 3H), 1.23 (m, 2H).
27.	**4-[(3-Chloro-4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.80 (d, J=2.2Hz, 1H), 7.57 (dd, J=2.2, 8.55 Hz, 1H), 7.25-7.4 (m, 5H), 7.05 (d, J=8.55 Hz, 1H), 6.13 (brt, 1H), 6.04 (brs,1H), 5.12 (s,2H), 4.22 (brs, 2H), 3.33 (brs, 2H), 2.78 (brs, 2H), 1.7-1.9 (m, 3H), 1.23 (m, 2H).

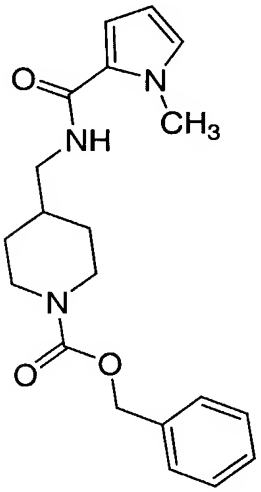
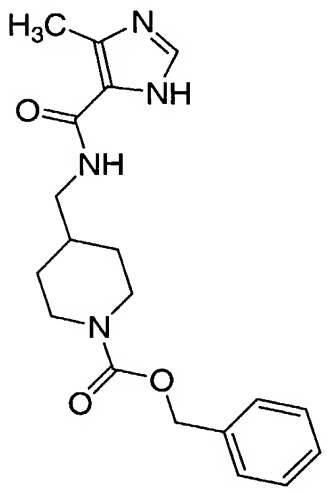
EX.	Name	Structure	Data
28.	**4-{[(Thiophene-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.84 (s, 1H), 7.41-7.27 (m, 7H), 6.24 (brt, 1H), 5.06 (s, 2H), 4.19 (brd, 2H), 3.30 (brs, 2H), 2.77 (brt, 2H), 1.9-1.7 (m, 3H), 1.18 (m, 2H).
29.	**4-{[(Thiazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 8.74 (d, 1H), 8.17 (d, 1H), 7.50 (brt, 1H), 7.26 (m, 5H), 5.11 (s, 2H), 4.19 (brs, 2H), 3.35 (brs, 2H), 2.78 (brt, 2H), 1.9-1.7 (m, 3H), 1.21 (m, 2H).

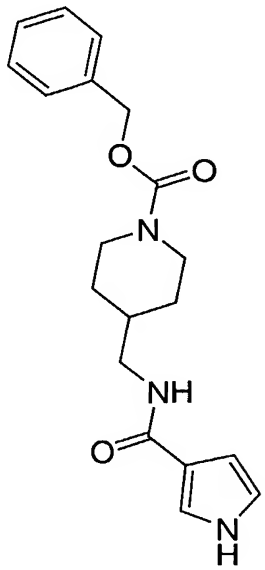
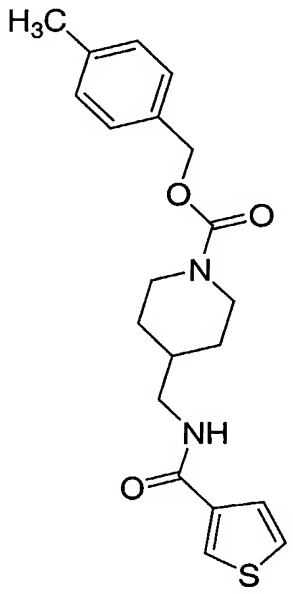
EX.	Name	Structure	Data
30.	**4-{[(2H-Pyrazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.59 (d, J=1.3Hz, 1H), 7.36-7.28 (m, 5H), 7.07 (brt, 1H), 6.82 (d, J=1.3Hz, 1H), 5.13 (s, 2H), 4.20 (brs, 2H), 3.37 (brs, 2H), 2.78 (brt, 2H), 1.9-1.7 (m, 3H), 1.21 (m, 2H).
31.	**4-{[(5-Oxo-4,5-dihydro-1H-[1,2,4]triazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		^{1}H NMR (500MHz, δ, $CDCl_3$): 11.55 (s, br, 2H), 7.45-7.30 (m, 6H), 5.12 (s, 2H), 4.19 (s, 2H), 3.25 (m, 2H), 2.75 (m, 2H), 1.85-1.65 (m, 3H), 1.15 (m, 2H).

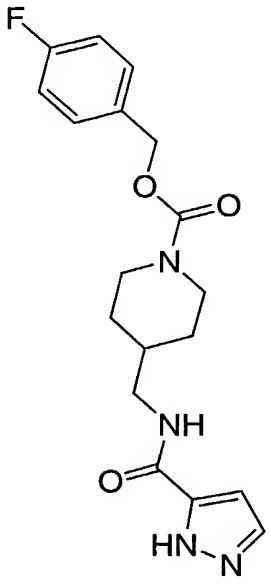
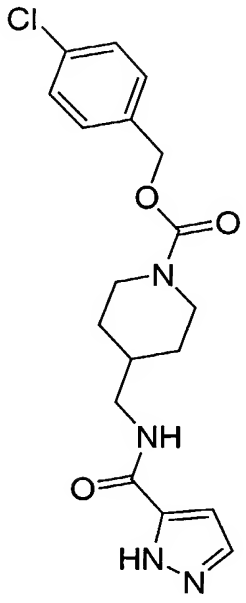
EX.	Name	Structure	Data
32.	**4-{[(2H-[1,2,4]Triazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		^{1}H NMR (500MHz, δ, DMSO-d_6): 14.60 (s, br, 1H), 8.80-8.30 (s, br, 2H), 7.40-7.30 (m, 5H), 5.07 (s, 2H), 3.98 (d, 2H), 3.15 (t, 2H), 2.77 (m, br, 2H), 1.77 (m, 1H), 1.63 (d, 2H), 1.05 (m, 2H).
33.	**4-{[(Thiazole-5-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		^{1}H NMR (500MHz, δ, DMSO-d_6): 9.21 (s, 1H), 8.74 (m, 1H), 8.46 (s, 1H), 7.40-7.28 (m, 5H), 5.09 (s, 2H), 4.00 (d, 2H), 3.12 (t, 2H), 2.90-2.70 (m, br, 2H), 1.80-1.65 (m, 3H), 1.05 (m, 2H).

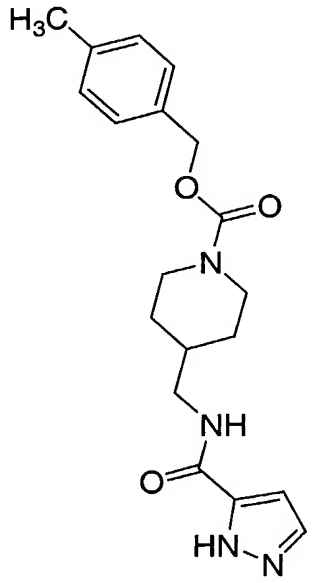
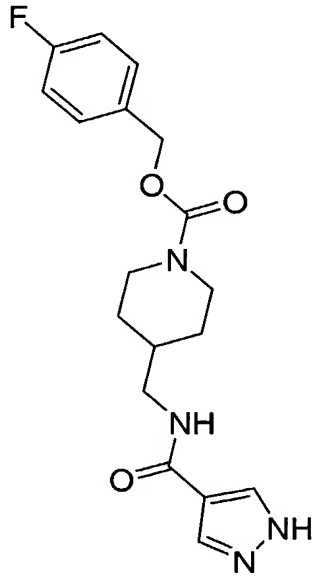
EX.	Name	Structure	Data
34.	**4-{[(1H-Pyrazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		^{1}H NMR (500MHz, δ, CD_3OD): 8.2-7.8 (s, br, 2H), 7.36-7.25 (m, 5H), 5.11 (s, 2H), 4.15 (m, 2H), 3.23 (m, 2H), 2.90-2.75 (s, br, 2H), 1.90-1.70 (m, 3H), 1.20-1.10 (m, 2H).
35.	**4-{[(2-Bromo-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		^{1}H NMR (500MHz, δ, DMSO-d_6): 8.88 (m, 1H), 8.54 (d, 1H), 7.99 (s, 1H), 7.78 (d, 1H), 7.38-7.28 (m, 5H), 5.07 (s, 1H), 4.00 (d, 2H), 3.16 (t, 2H), 2.90-2.70 (m, 2H), 1.80-1.65 (m, 3H), 1.09 (m, 2H).

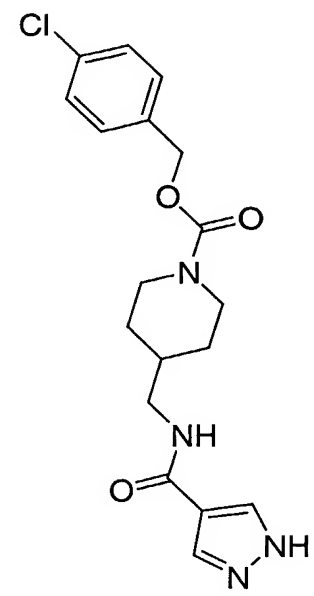
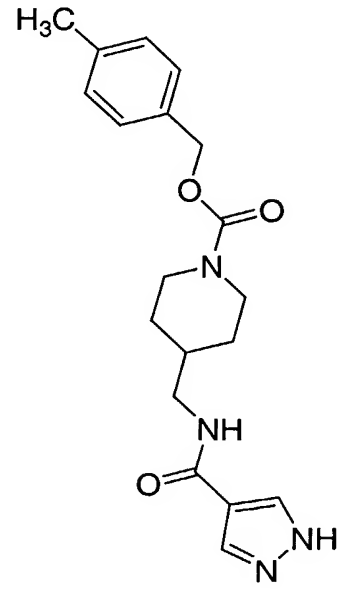
EX.	Name	Structure	Data
36.	**4-{[(1H-Pyrrole-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 9.55 (brs, 1H), 7.39-7.28 (m, 5H), 6.92 (m, 1H), 6.57 (m, 1H), 6.22 (m, 1H), 6.01 (brt, 1H), 5.08 (s, 2H), 4.20 (brs, 2H), 3.28 (brs, 2H), 2.77 (brt, 2H), 1.9-1.7 (m, 3H), 1.21 (m, 2H).
37.	**4-{[(1H-Imidazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.58 (m, 2H), 7.38-7.27 (m, 5H), 5.10 (s, 2H), 4.20 (brd, 2H), 3.37 (brs, 2H), 2.77 (brt, 2H), 1.9-1.7 (m, 3H), 1.21 (m, 2H).

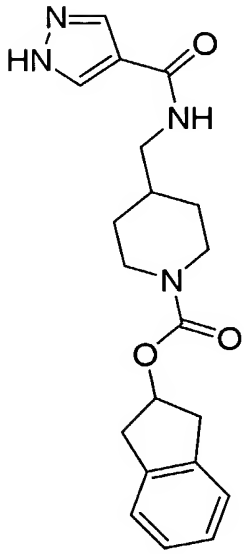
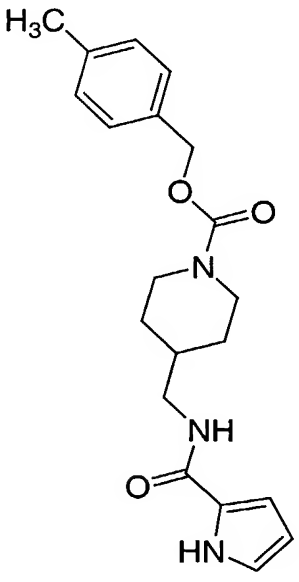
EX.	Name	Structure	Data
38.	**4-{[(1-Methyl-1H-pyrrole-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.38-7.25 (m, 5H), 6.71 (m, 1H), 6.50 (m, 1H), 6.08 (m, 1H), 6.00 (brt, 1H), 5.11 (s, 2H), 4.22 (brs, 2H), 3.94 (s, 3H), 3.26 (brs, 2H), 2.77 (brt, 2H), 1.9-1.7 (m, 3H), 1.21 (m, 2H).
39.	**4-{[(5-Methyl-3H-imidazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 9.62 (brs, 1H), 7.40 (s, 1H), 7.31 (m, 6H), 5.12 (s, 2H), 4.19 (brd, 2H), 3.25 (brs, 2H), 2.77 (brt, 2H), 2.59 (s, 3H), 1.9-1.7 (m, 3H), 1.21 (m, 2H).

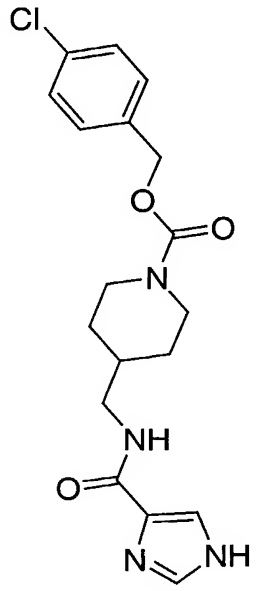
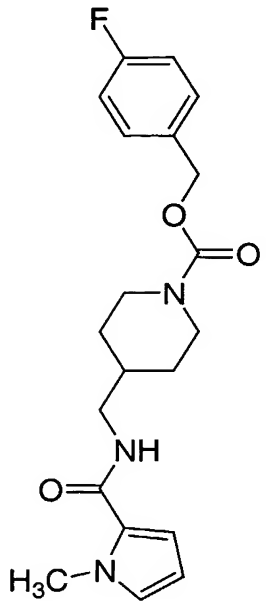
EX.	Name	Structure	Data
40.	**4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 8.55 (brs, 1H), 7.28 (m, 6H), 6.78 (s, 1H), 6.40 (s, 1H), 5.88 (brt, 1H), 5.10 (s, 2H), 4.19 (brs, 2H), 3.30 (brs, 2H), 2.77 (brt, 2H), 1.9-1.7 (m, 3H), 1.20 (m, 2H).
41.	**4-{[(Thiophene-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.83 (m, 1H), 7.38 (m, 2H), 7.24 (d, 2H), 7.18 (d, 2H), 6.19 (brt, 1H), 5.02 (s, 2H), 4.20 (brs, 2H), 3.30 (brs, 2H), 2.77 (brt, 2H), 2.35 (s, 3H), 1.9-1.7 (m, 3H), 1.21 (m, 2H).

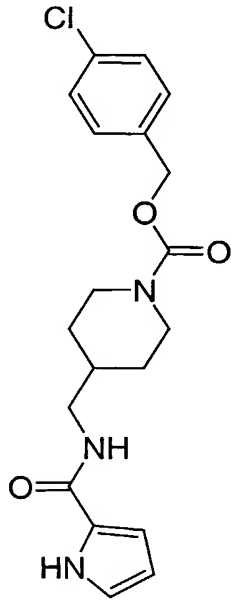
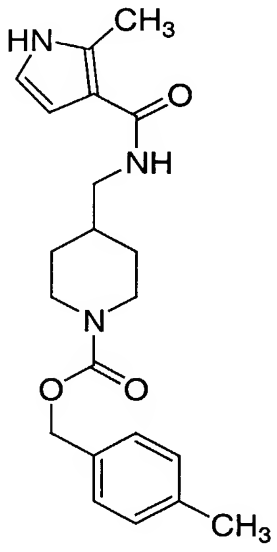
EX.	Name	Structure	Data
42.	**4-{[(2H-Pyrazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-fluoro-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.60 (d, 1H), 7.30 (d, 2H), 7.04 (m, 3H), 6.82 (d, 1H), 5.04 (s, 2H), 4.18 (brs, 2H), 3.33 (brs, 2H), 2.77 (brt, 2H), 1.9-1.7 (m, 3H), 1.21 (m, 2H).
43.	**4-{[(2H-Pyrazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-chloro-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.58 (d, 1H), 7.27 (m, 4H), 7.04 (brt, 1H), 6.82 (d, 1H), 5.05 (s, 2H), 4.18 (brs, 2H), 3.36 (brs, 2H), 2.77 (brt, 2H), 1.9-1.7 (m, 3H), 1.21 (m, 2H).

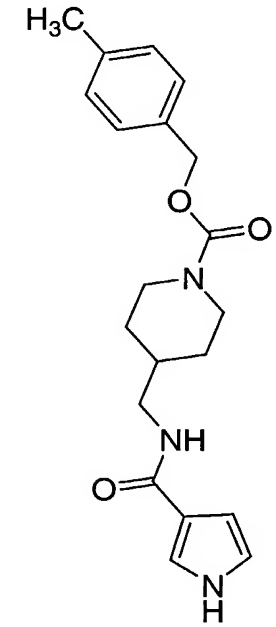
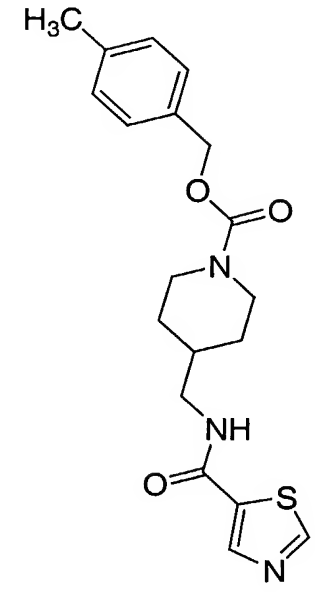
EX.	Name	Structure	Data
44.	**4-{[(2H-Pyrazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.60 (d, 1H), 7.22 (d, 2H), 7.17 d, 2H), 6.97 (brt, 1H), 6.84 (d, 1H),, 5.04 (s, 2H), 4.20 (brs, 2H), 3.35 (brs, 2H), 2.77 (brt, 2H), 2.37 (m, 3H), 1.9-1.7 (m, 3H), 1.21 (m, 2H).
45.	**4-{[(1H-Pyrazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-fluoro-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.94 (s, 2H), 7.30 (m, 2H), 7.01 (m, 2H), 6.60 (brs, 1H), 5.03 (s, 2H), 4.16 (brd, 2H), 3.24 (brs, 2H), 2.75 (brs, 2H), 1.9-1.7 (m, 3H), 1.15 (m, 2H).

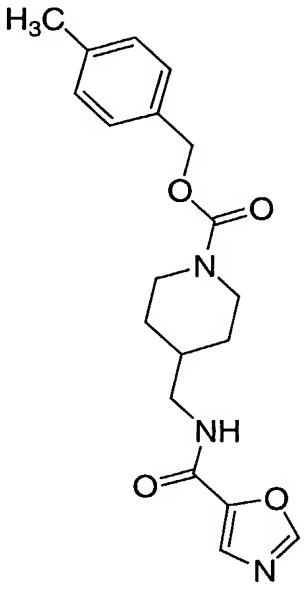
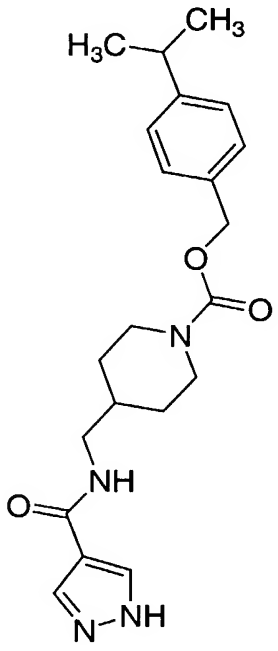
EX.	Name	Structure	Data
46.	**4-{[(1H-Pyrazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-chloro-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.94 (s, 2H), 7.26 (m, 4H), 6.43 (brs, 1H), 5.03 (s, 2H), 4.17 (brs, 2H), 3.25 (brs, 2H), 2.77 (brs, 2H), 1.9-1.7 (m, 3H), 1.15 (m, 2H).
47.	**4-{[(1H-Pyrazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.94 (s, 2H), 7.25 (d, 2H), 7.16 (d, 2H), 6.03 (brt, 1H), 5.06 (s, 2H), 4.20 (brs, 2H), 3.30 (brs, 2H), 2.77 (brt, 2H), 2.37 (s, 3H), 1.9-1.7 (m, 3H), 1.20 (m, 2H).

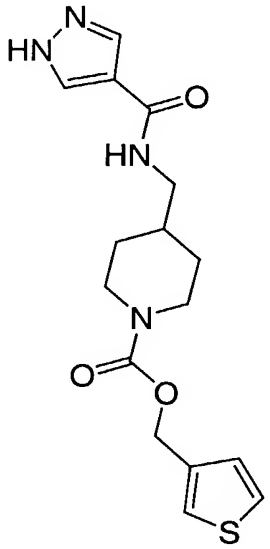
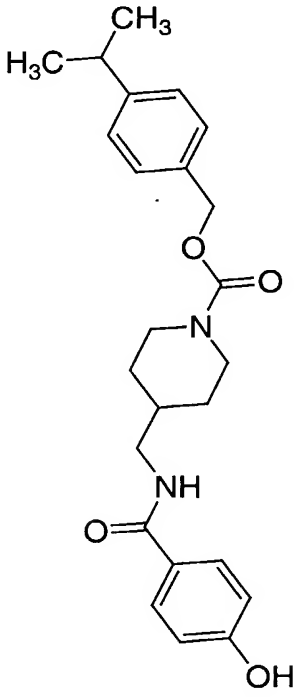
EX.	Name	Structure	Data
48.	**4-{[(1H-Pyrazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid indan-2-yl ester**		^{1}H NMR (δ, $CDCl_3$): 7.94 (s, 2H), 7.20 (m, 4H), 6.15 (brt, 1H), 5.42 (m,1H), 4.10 (brd, 2H), 3.30 (m, 4H), 3.00 (dd, 2H), 2.70 (t, 2H), 1.8-1.6 (m, 3H), 1.18 (m, 2H).
49.	**4-{[(1H-Pyrrole-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 9.43 (brs, 1H), 7.24 (d, 2H), 7.17 (d, 2H), 6.91 (s, 1H), 6.55 (s, 1H), 6.22 (m, 1H), 5.95 (brt, 1H), 5.06 (s, 2H), 4.19 (brs, 2H), 3.30 (brs, 2H), 2.77 (brt, 2H), 2.36 (s, 3H), 1.9-1.7 (m, 3H), 1.18 (m, 2H).

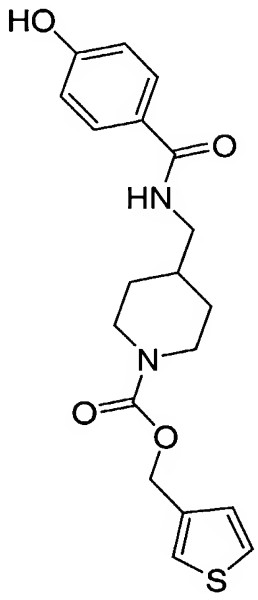
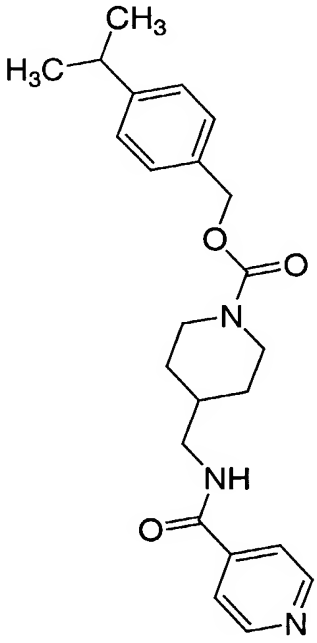
EX.	Name	Structure	Data
50.	**4-{[(1H-Imidazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-chloro-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.59 (s, 2H), 7.30 (m, 5H), 5.06 (s, 2H), 4.18 (brs, 2H), 3.33 (brs, 2H), 2.77 (brt, 2H), 1.9-1.7 (m, 3H), 1.21 (m, 2H).
51.	**4-{[(1-Methyl-1H-pyrrole-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-fluoro-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.31 (dd, 2H), 7.02 (dd, 2H), 6.72 (s, 1H), 6.50 (m, 1H), 6.08 (m, 1H), 6.00 (brt, 1 H), 5.04 (s, 2H), 4.18 (brs, 2H), 3.93 (s, 3H), 3.25 (brs, 2H), 2.77 (brt, 2H), 1.9-1.7 (m, 3H), 1.18 (m, 2H).

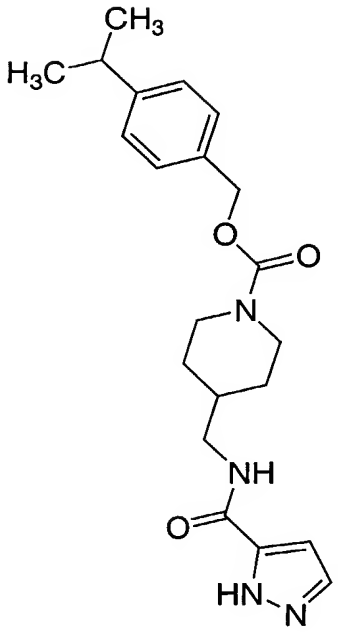
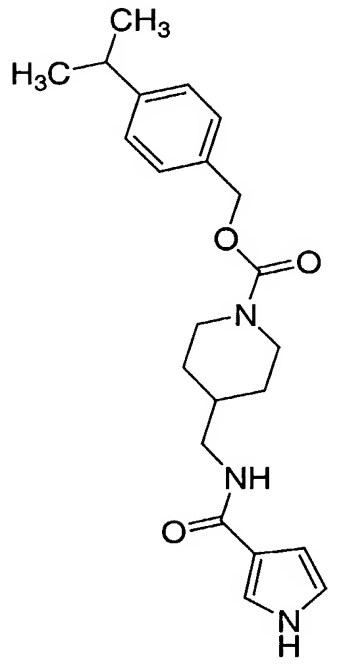
EX.	Name	Structure	Data
52.	**4-{[(1H-Pyrrole-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-chloro-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 9.37 (brs, 1H), 7.24 (m, 4H), 6.92 (s, 1H), 6.53 (s, 1H), 6.22 (m, 1H), 5.93 (brt, 1H), 5.06 (s, 2H), 4.20 (brs, 2H), 3.31 (brs, 2H), 2.77 (brt, 2H), 1.9-1.7 (m, 3H), 1.18 (m, 2H).
53.	**4-{[(2-Methyl-1H-pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 8.10 (brs, 1H), 7.25 (d, 2H), 7.17 (d, 2H), 6.59 (m, 1H), 6.23 (m, 1H), 5.81 (brt, 1H), 5.06 (s, 2H), 4.20 (brs, 2H), 3.26 (brs, 2H), 2.77 (brt, 2H), 2.55 (s, 3H), 2.36 (s, 3H), 1.9-1.7 (m, 3H), 1.20 (m, 2H).

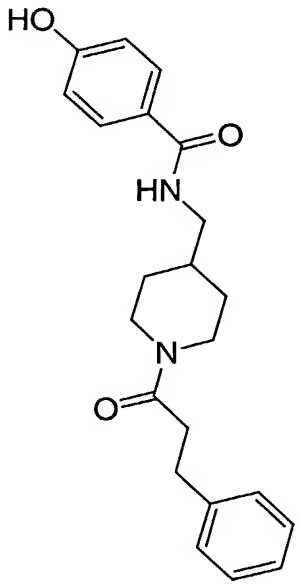
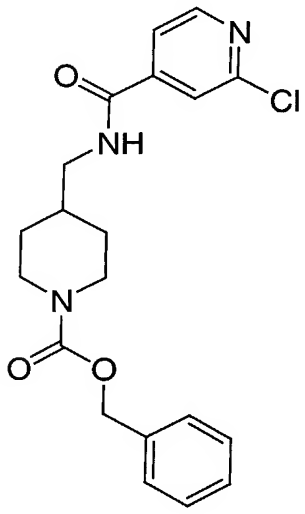
EX.	Name	Structure	Data
54.	**4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 8.55 (brs, 1H), 7.36 (m, 1H), 7.25 (d, 2H), 7.17 (d, 2H), 6.77 (m, 1H), 6.40 (m, 1H), 5.86 (brt, 1H), 5.06 (s, 2H), 4.19 (brs, 2H), 3.29 (brs, 2H), 2.77 (brt, 2H),2.36 (s, 3H), 1.9-1.7 (m, 3H), 1.18 (m, 2H).
55.	**4-{[(Thiazole-5-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 8.90 (s, 1H), 8.24 (s, 1H), 7.24 (d, 2H), 7.16 (d, 2H), 6.24 (brt, 1H), 5.05 (s, 2H), 4.20 (brs, 2H), 3.35 (brs, 2H), 2.77 (brt, 2H), 2.36 (s, 3H), 1.9-1.7 (m, 3H), 1.21 (m, 2H).

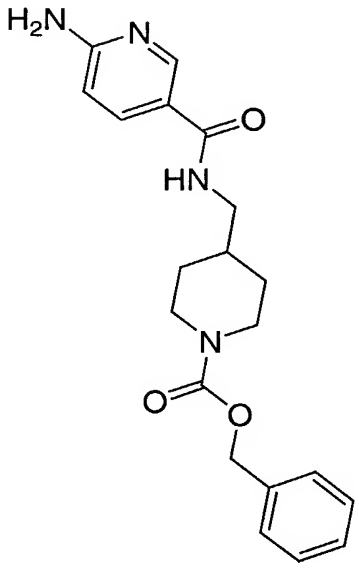
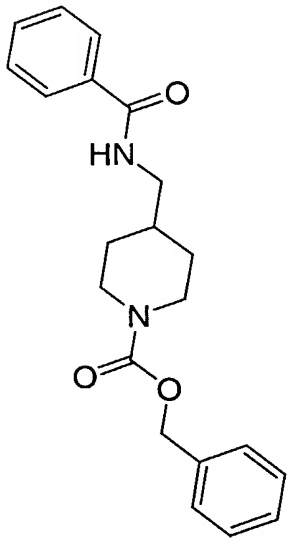
EX.	Name	Structure	Data
56.	**4-{[(Oxazole-5-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.90 (s, 1H), 7.72 (s, 1H), 7.23 (d, 2H), 7.17 (d, 2H), 6.35 (brt, 1H), 5.05 (s, 2H), 4.20 (brs, 2H), 3.33 (brs, 2H), 2.77 (brt, 2H), 2.35 (s, 3H), 1.9-1.7 (m, 3H), 1.20 (m, 2H).
57.	**4-{[(1H-Pyrazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-isopropyl-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.93 (s, 2H), 7.25 (m, 4H), 6.62 (brt, 1H), 5.07 (s, 2H), 4.16 (brd, 2H), 3.26 (brs, 2H), 2.89 (m, 1H), 2.71 (brt, 2H), 1.9-1.7 (m, 3H), 1.23 (d, 6H), 1.18 (m, 2H).

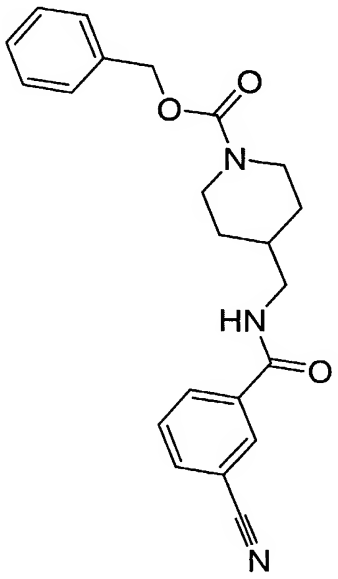
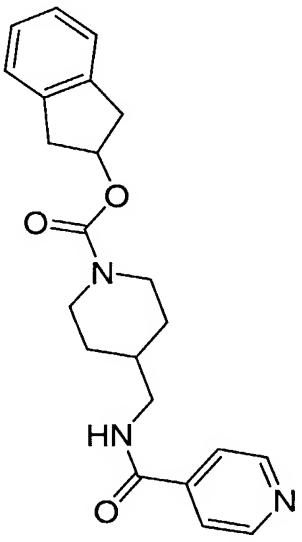
EX.	Name	Structure	Data
58.	**4-{[(1H-Pyrazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid thiophen-3-ylmethyl ester**		^{1}H NMR (δ, $CDCl_3$): 10.50 (brs, 1H), 7.94 (s, 2H), 7.28 (m, 2H), 7.08 (m, 1H), 5.93 (brt, 1H), 5.11 (s, 2H), 4.19 (brs, 2H), 3.31 (brs, 2H), 2.77 (brt, 2H), 1.9-1.7 (m, 3H), 1.19 (m, 2H).
59.	**4-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid 4-isopropyl-benzyl ester**		^{1}H NMR (δ, CD_3OD): 8.24 (brd, 1H) 7.68 (d, 2H), 7.20 (m, 4H), 6.79 (d, 2H), 5.02 (s, 2H), 4.10 (d, 2H), 3.20 (t, 2H), 2.81 (m, 1H), 2.77 (brs, 2H), 1.77 (m, 1H), 1.70 (brd, 2H), 1.20 (d, 6H), 1.16 (m, 2H).

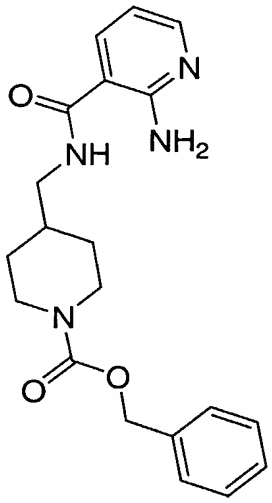
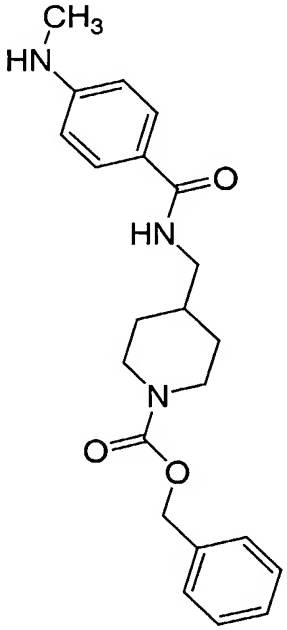
EX.	Name	Structure	Data
60.	**4-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid thiophen-3-ylmethyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.94 (s, 2H), 7.26 (m, 4H), 7.09 (d, 1H), 5.92 (brt, 1H), 5.14 (s, 2H), 4.19 (brs, 2H), 3.30 (brs, 2H), 2.77 (brt, 2H), 1.9-1.7 (m, 3H), 1.20 (m, 2H).
61.	**4-{[(Pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-isopropyl-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 8.72 (d, 2H), 7.60 (d, 2H), 7.22 (m, 4H), 6.55 (brt, 1H), 5.06 (s, 2H), 4.21 (brd, 2H), 3.33 (brs, 2H), 2.90 (m, 1H), 2.77 (brt, 2H), 1.9-1.7 (m, 3H), 1.21 (d, 6H), 1.18 (m, 2H).

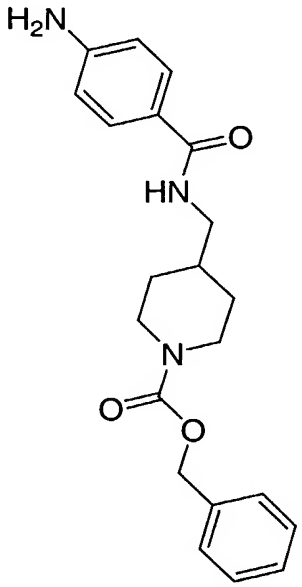
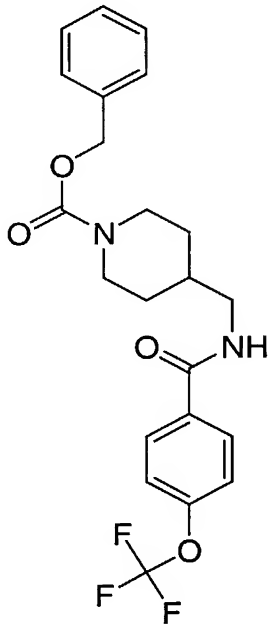
EX.	Name	Structure	Data
62.	**4-{[(2H-Pyrazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-isopropyl-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 7.57 (m, 1H), 7.23 (m, 4H),7.02 (brt, 1H), 6.83 (m, 1H), 5.06 (s, 2H), 4.19 (brs, 2H), 3.33 (brs, 2H), 2.90 (m, 1H), 2.77 (brt, 2H), 1.9-1.7 (m, 3H), 1.21 (d, 6H), 1.18 (m, 2H).
63.	**4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-isopropyl-benzyl ester**		^{1}H NMR (δ, $CDCl_3$): 9.79 (brs, 1H), 7.30-7.15 (m, 5H), 6.70 (s, 1H), 6.42 (s, 1H), 6.30 (brt, 1H), 5.06 (s, 2H), 4.17 (brs, 2H), 3.25 (brs, 2H), 2.90 (m, 1H), 2.75 (brs, 2H), 1.9-1.7 (m, 3H), 1.22 (d, 6H), 1.17 (m, 2H).

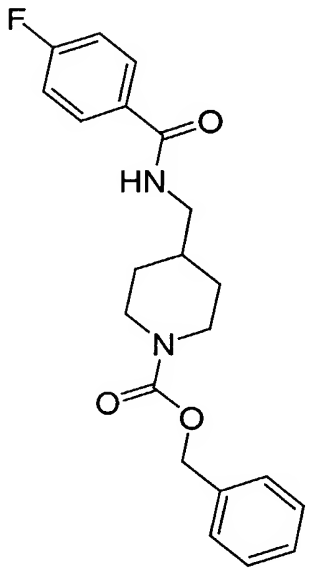
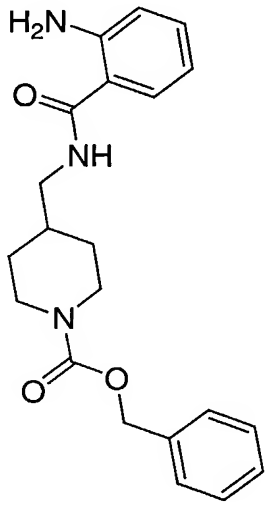
EX.	Name	Structure	Data
64.	**4-Hydroxy-N-[1-(3-phenyl-propionyl)-piperidin-4-ylmethyl]-benzamide**		^{1}H NMR (δ, $CDCl_3$): 8.80 (brs, 1H), 7.63 (d, 2H), 7.3-7.1 (m, 5H), 6.89 (d, 2H), 6.69 (brt, 1H), 4.58 (d, 1H), 3.76 (d, 1H), 3.35-3.18 (m, 2H), 2.90 (m, 3H), 2.60 (t, 2H), 2.49 (t, 1H), 1.9-1.7 (m, 3H), 1.1-0.9 (m, 2H).
65.	**4-{[(2-Chloro-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 388

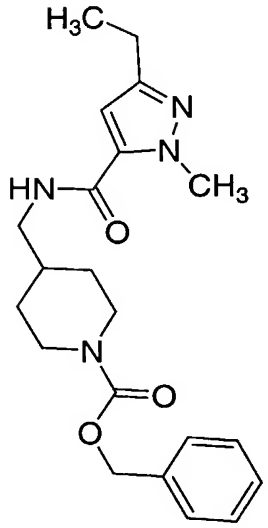
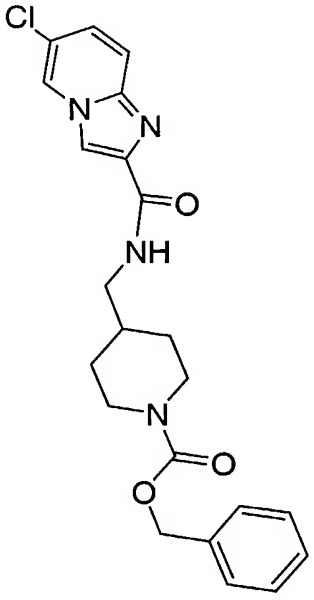
EX.	Name	Structure	Data
66.	**4-{[(6-Amino-pyridine-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 369
67.	**4-(Benzoylamino-methyl)-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 353

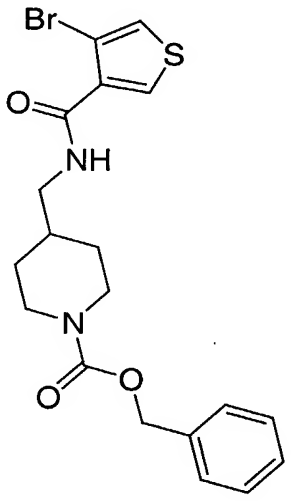
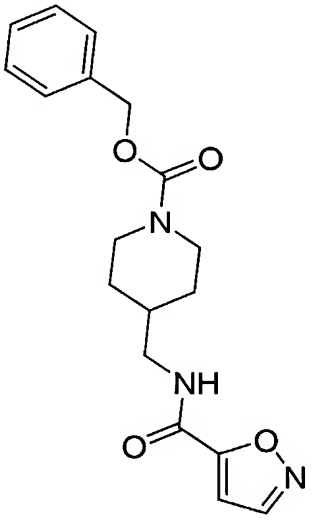
EX.	Name	Structure	Data
68.	**4-[(3-Cyano-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 378
69.	**4-{[(Pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid indan-2-yl ester**		M.S. (M^++1) 380

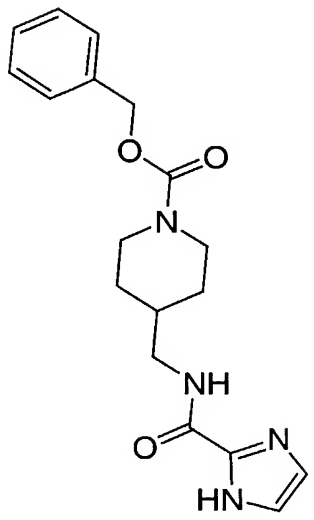
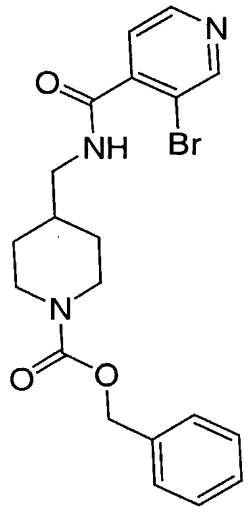
EX.	Name	Structure	Data
70.	**4-{[(2-Amino-pyridine-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 369
71.	**4-[(4-Methylamino-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 382

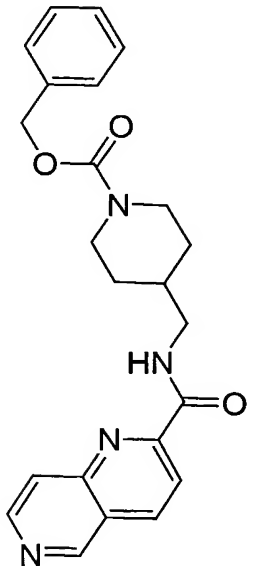
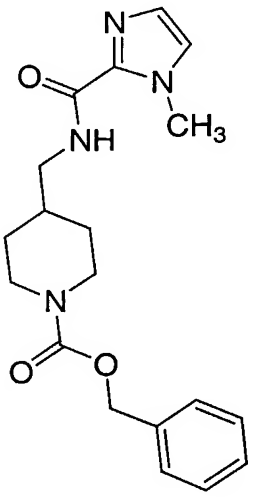
EX.	Name	Structure	Data
72.	**4-[(4-Amino-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 368
73.	**4-[(4-Trifluoromethoxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 437

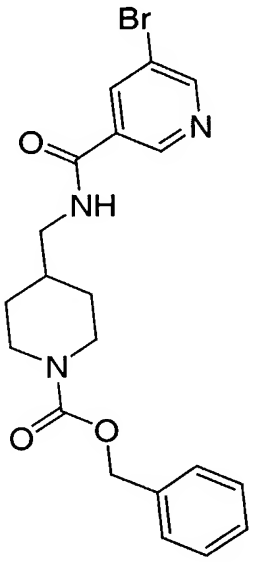
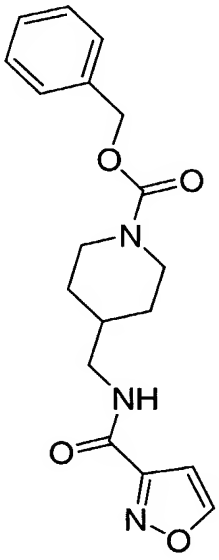
EX.	Name	Structure	Data
74.	**4-[(4-Fluoro-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 371
75.	**4-[(2-Amino-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 368

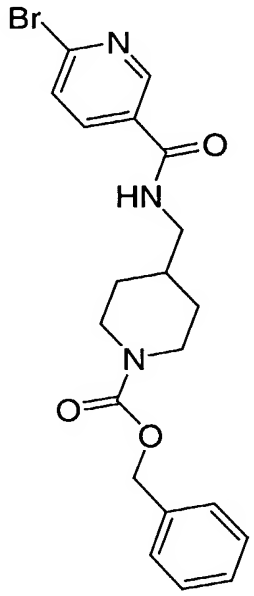
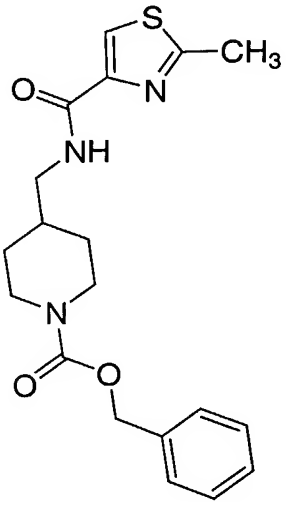
EX.	Name	Structure	Data
76.	**4-{[(5-Ethyl-2-methyl-2H-pyrazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 385
77.	**4-{[(6-Chloro-imidazo[1,2-a]pyridine-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 427

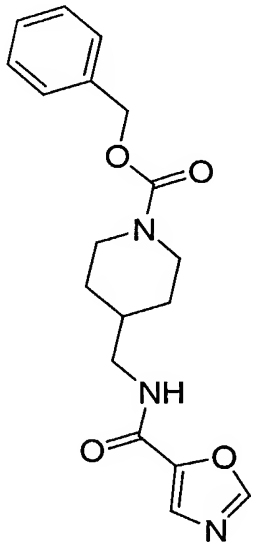
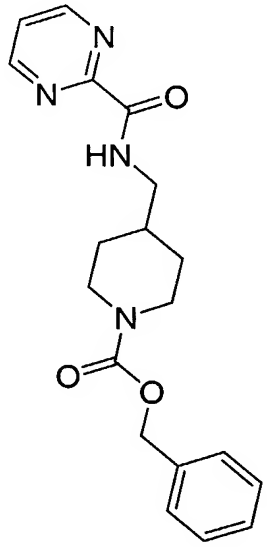
EX.	Name	Structure	Data
78.	**4-{[(4-Bromo-thiophene-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 438
79.	**4-{[(Isoxazole-5-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 344

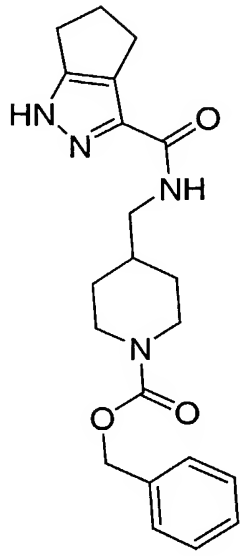
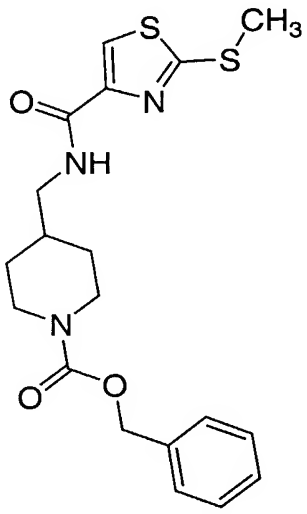
EX.	Name	Structure	Data
80.	**4-{[(1H-Imidazole-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 343
81.	**4-{[(3-Bromo-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 433

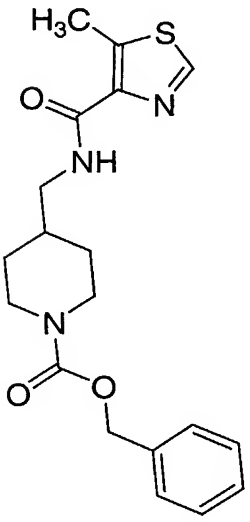
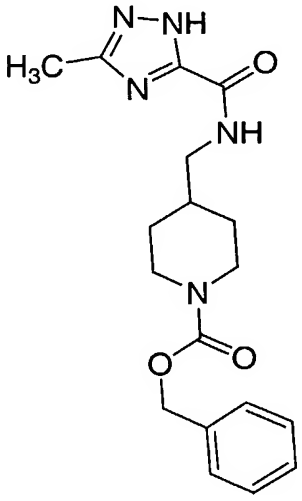
EX.	Name	Structure	Data
82.	**4-{[([1,6]Naphthyridine-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 405
83.	**4-{[(1-Methyl-1H-imidazole-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 357

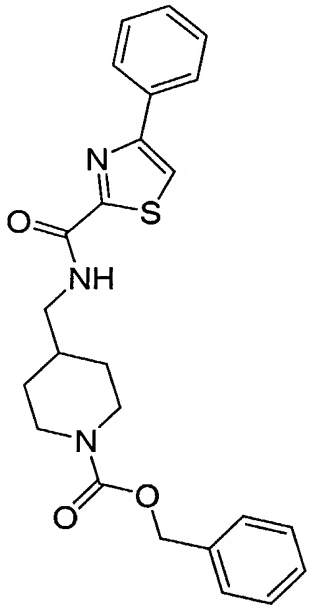
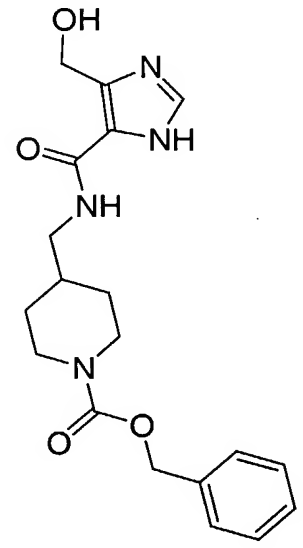
EX.	Name	Structure	Data
84.	**4-{[(5-Bromo-pyridine-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 432
85.	**4-{[(Isoxazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 344

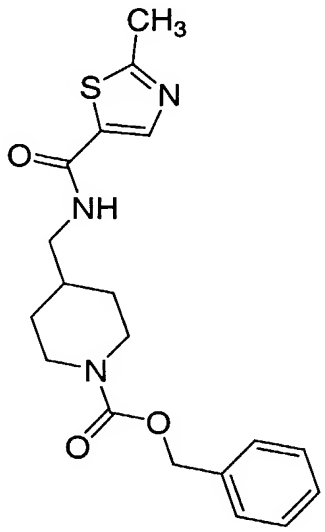
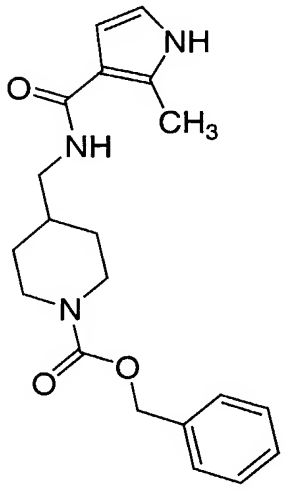
EX.	Name	Structure	Data
86.	**4-{[(6-Bromo-pyridine-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 432
87.	**4-{[(2-Methyl-thiazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 374

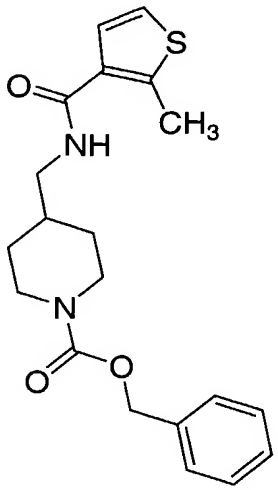
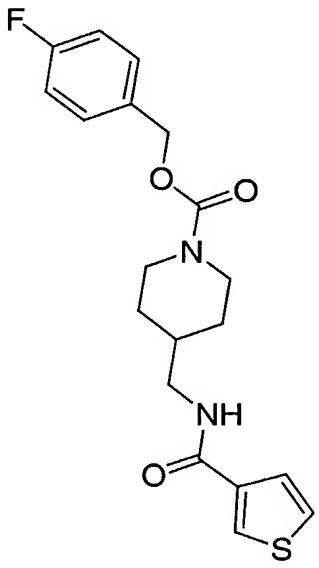
EX.	Name	Structure	Data
88.	**4-{[(Oxazole-5-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 344
89.	**4-{[(Pyrimidine-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 355

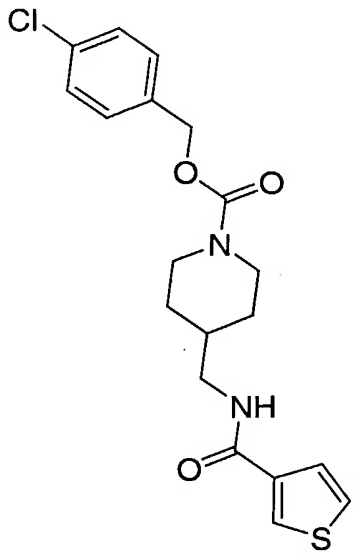
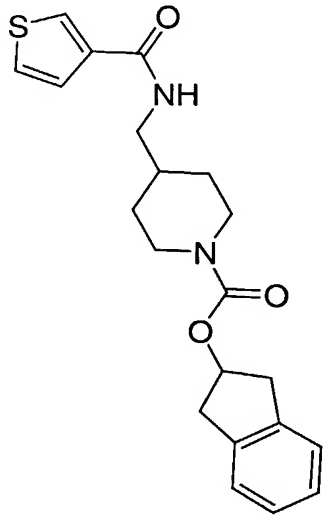
EX.	Name	Structure	Data
90.	**4-{[(1,4,5,6-Tetrahydro-cyclopentapyrazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 383
91.	**4-{[(2-Methylsulfanyl-thiazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 406

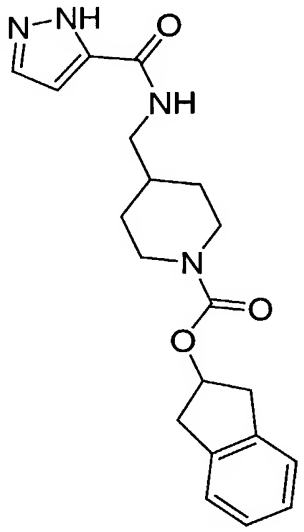
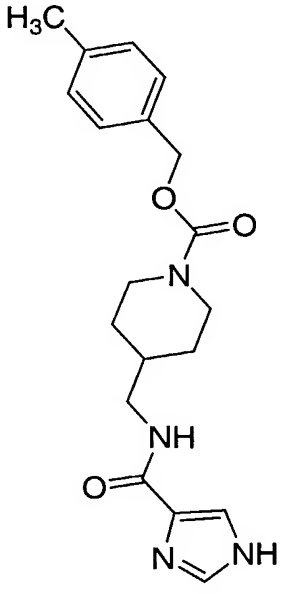
EX.	Name	Structure	Data
92.	**4-{[(5-Methyl-thiazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 374
93.	**4-{[(5-Methyl-2H-[1,2,4]triazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 358

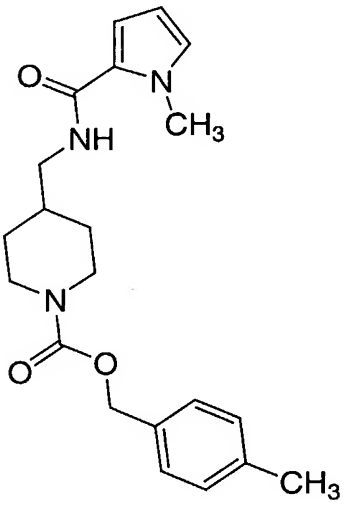
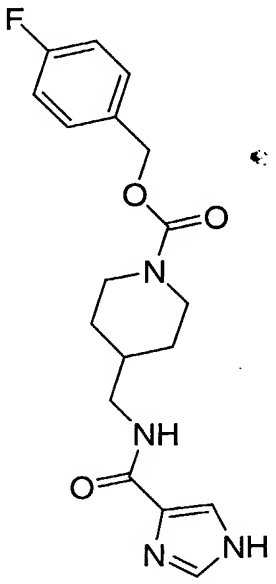
EX.	Name	Structure	Data
94.	4-{[(4-Phenyl-thiazole-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester		M.S. (M^++1) 436
95.	4-{[(5-Hydroxymethyl-3H-imidazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester		M.S. (M^++1) 373

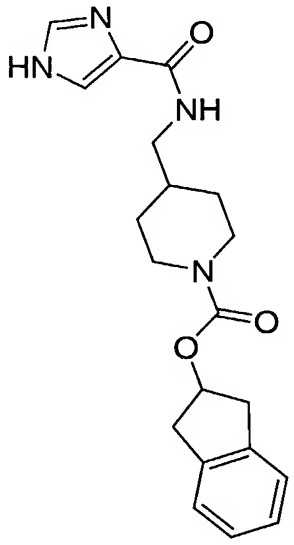
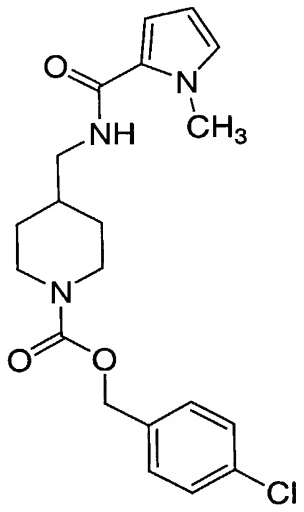
EX.	Name	Structure	Data
96.	4-{[(2-Methyl-thiazole-5-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester		M.S. (M^++1) 374
97.	4-{[(2-Methyl-1H-pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester		M.S. (M^++1) 356

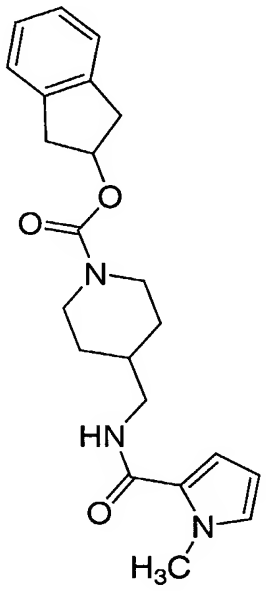
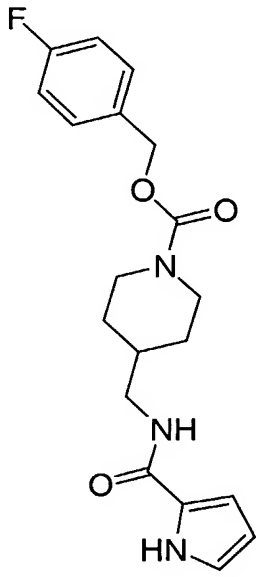
EX.	Name	Structure	Data
98.	**4-{[(2-Methyl-thiophene-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 373
99.	**4-{[(Thiophene-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-fluoro-benzyl ester**		M.S. (M^++1) 377

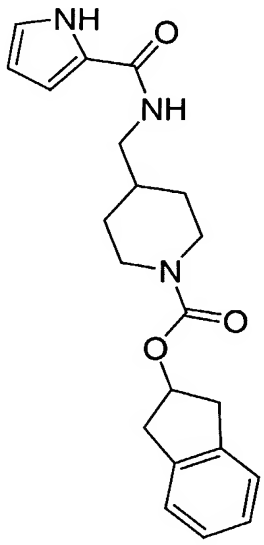
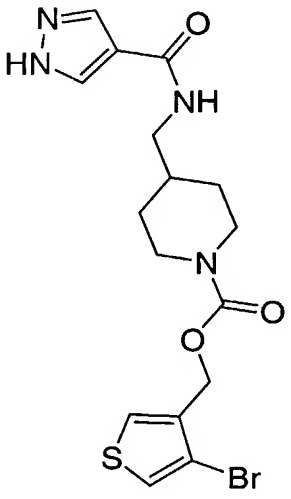
EX.	Name	Structure	Data
100.	4-{[(Thiophene-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-chloro-benzyl ester		M.S. (M^++1) 393
101.	4-{[(Thiophene-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid indan-2-yl ester		M.S. (M^++1) 385

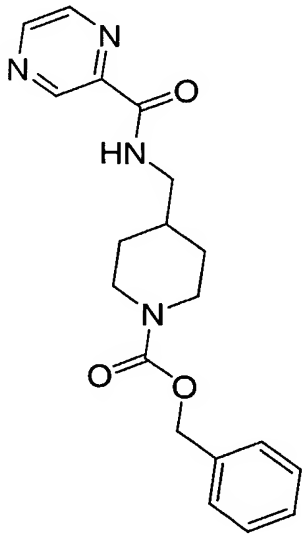
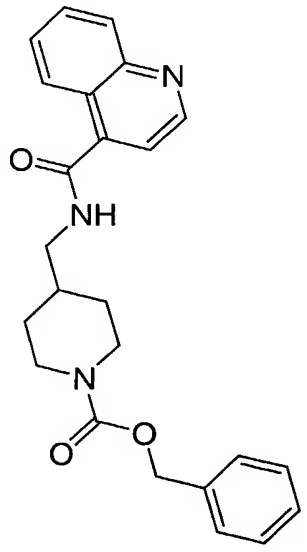
EX.	Name	Structure	Data
102.	**4-{[(2H-Pyrazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid indan-2-yl ester**		M.S. (M^++1) 369
103.	**4-{[(1H-Imidazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester**		M.S. (M^++1) 357

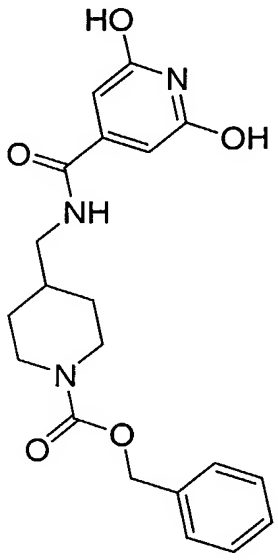
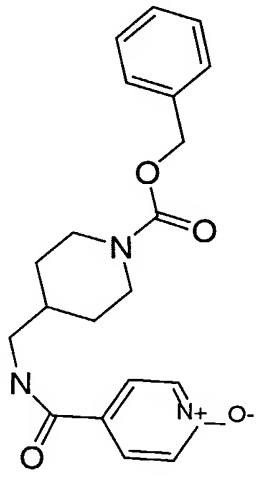
EX.	Name	Structure	Data
104.	4-{[(1-Methyl-1H-pyrrole-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester		M.S. (M^++1) 370
105.	4-{[(1H-Imidazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-fluoro-benzyl ester		M.S. (M^++1) 361

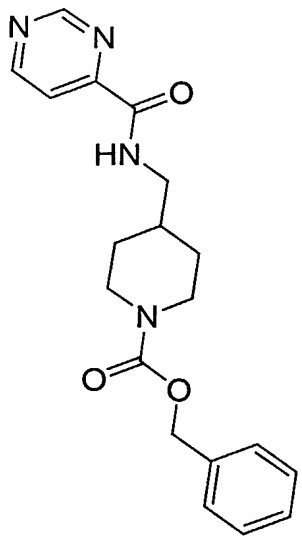
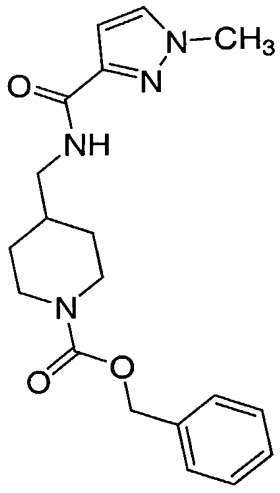
EX.	Name	Structure	Data
106.	**4-{[(1H-Imidazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid indan-2-yl ester**		M.S. (M^++1) 369
107.	**4-{[(1-Methyl-1H-pyrrole-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-chloro-benzyl ester**		M.S. (M^++1) 390

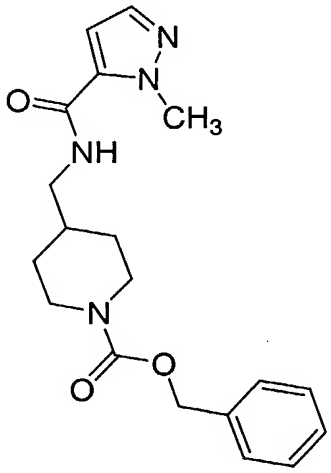
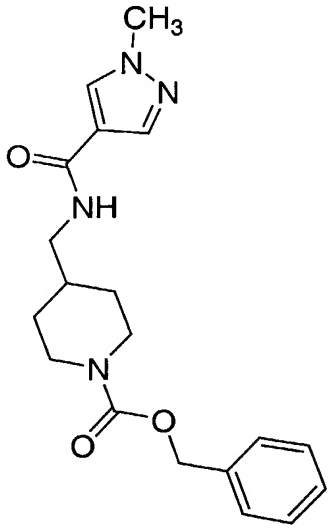
EX.	Name	Structure	Data
108.	**4-{[(1-Methyl-1H-pyrrole-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid indan-2-yl ester**		M.S. (M^++1) 382
109.	**4-{[(1H-Pyrrole-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-fluoro-benzyl ester**		M.S. (M^++1) 360

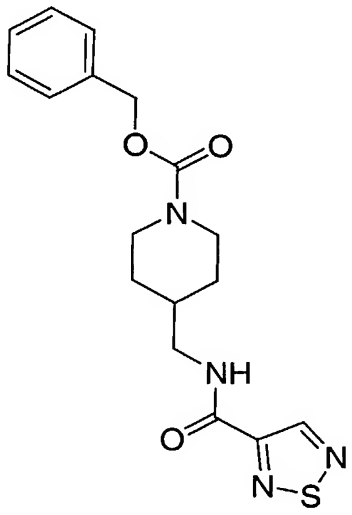
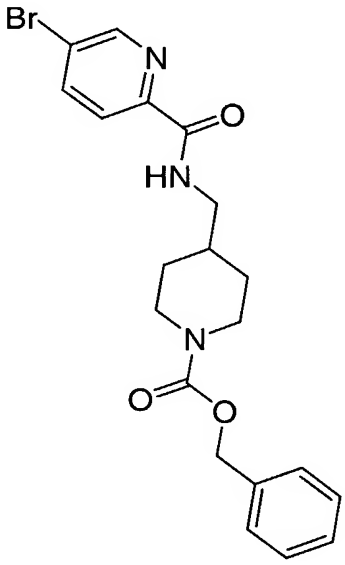
EX.	Name	Structure	Data
110.	**4-{[(1H-Pyrrole-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid indan-2-yl ester**		M.S. (M^++1) 368
111.	**4-{[(1H-Pyrazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-bromo-thiophen-3-ylmethyl ester**		M.S. (M^++1) 427

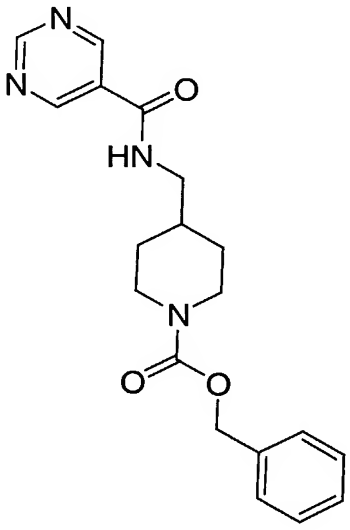
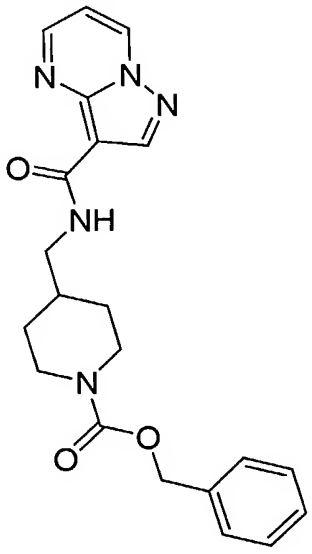
EX.	Name	Structure	Data
112.	**4-{[(Pyrazine-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 355
113.	**4-{[(Quinoline-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 404

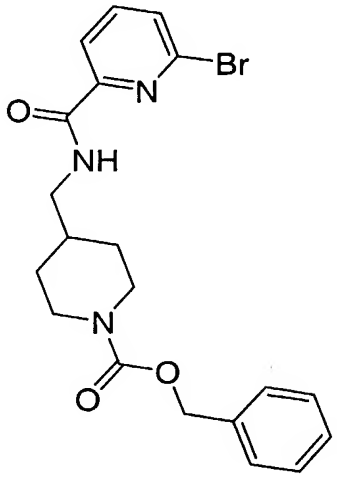
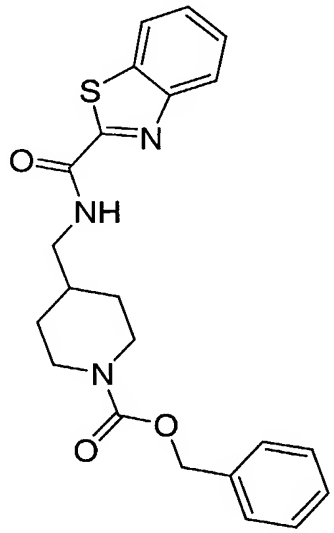
EX.	Name	Structure	Data
114.	**4-{[(2,6-Dihydroxy-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 386
115.	**4-{[(1-Oxy-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 370

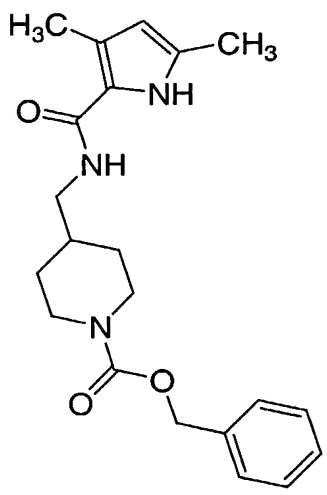
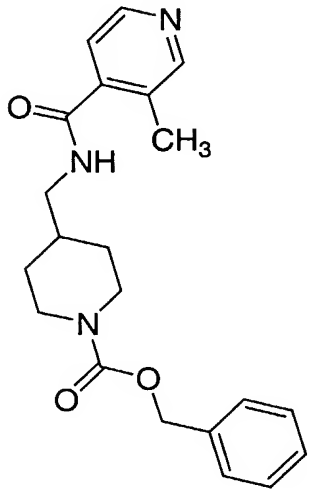
EX.	Name	Structure	Data
116.	**4-{[(Pyrimidine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 355
117.	**4-{[(1-Methyl-1H-pyrazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 357

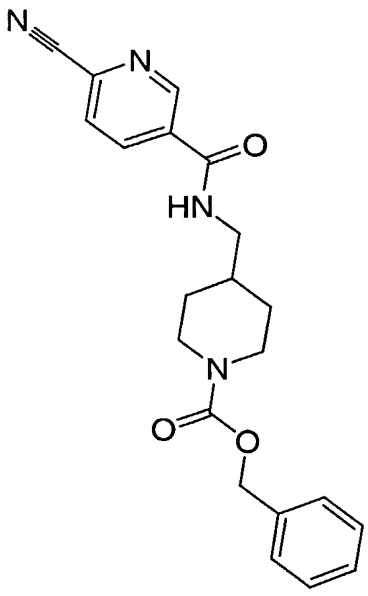
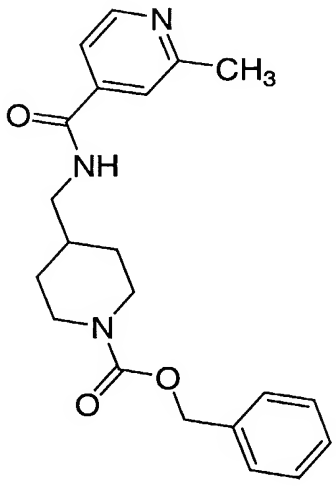
EX.	Name	Structure	Data
118.	**4-{[(2-Methyl-2H-pyrazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 357
119.	**4-{[(1-Methyl-1H-pyrazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 357

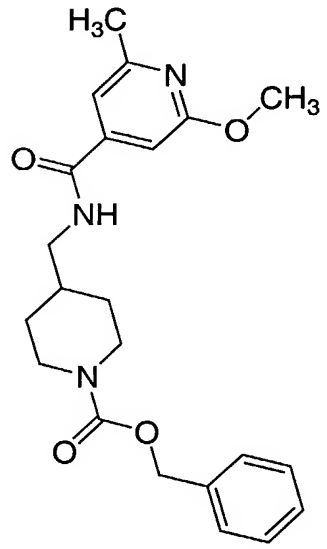
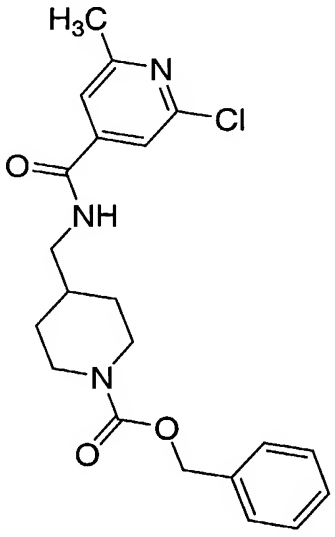
EX.	Name	Structure	Data
120.	**4-{[([1,2,5]Thiadiazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 361
121.	**4-{[(5-Bromo-pyridine-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 432

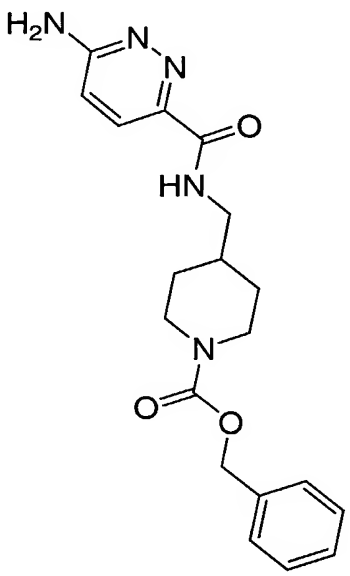
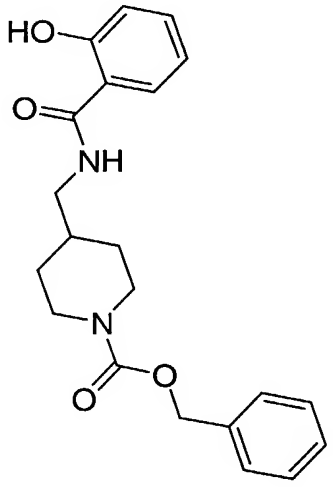
EX.	Name	Structure	Data
122.	**4-{[(Pyrimidine-5-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 355
123.	**4-{[(Pyrazolo[1,5-a]pyrimidine-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 394

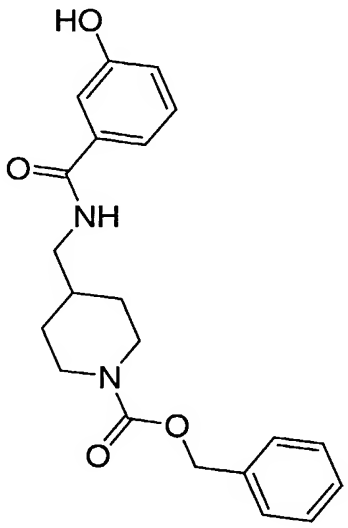
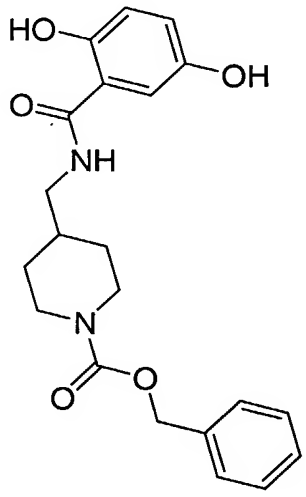
EX.	Name	Structure	Data
124.	**4-{[(6-Bromo-pyridine-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 432
125.	**4-{[(Benzothiazole-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 410

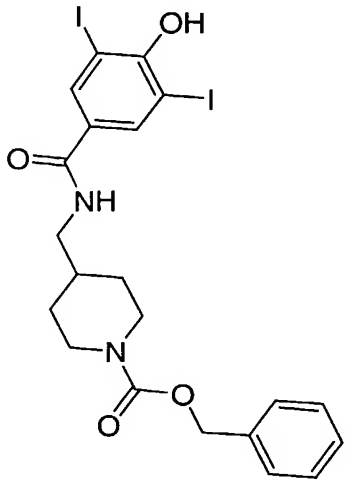
EX.	Name	Structure	Data
126.	**4-{[(3,5-Dimethyl-1H-pyrrole-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 370
127.	**4-{[(3-Methyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 368

EX.	Name	Structure	Data
128.	4-{[(6-Cyano-pyridine-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester		M.S. (M^++1) 379
129.	4-{[(2-Methyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester		M.S. (M^++1) 368

EX.	Name	Structure	Data
130.	**4-{[(2-Methoxy-6-methyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 398
131.	**4-{[(2-Chloro-6-methyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 402

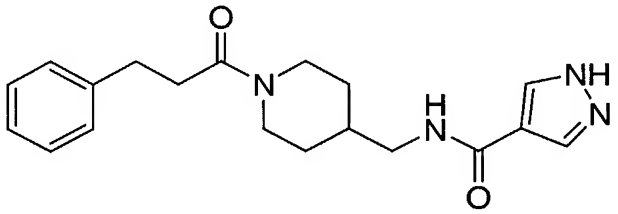
EX.	Name	Structure	Data
132.	**4-{[(6-Amino-pyridazine-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 370
133.	**4-[(2-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 369

EX.	Name	Structure	Data
134.	**4-[(3-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 369
135.	**4-[(2,5-Dihydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 385

EX.	Name	Structure	Data
136.	4-[(4-Hydroxy-3,5-diiodo-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester		M.S. (M^++1) 621

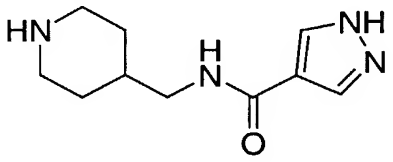
EXAMPLE 137:

1H-Pyrazole-4-carboxylic acid [1-(3-phenyl-propionyl)-piperidin-4-ylmethyl]-amide



Step 1:

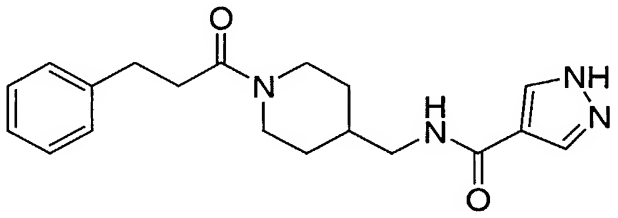
1H-Pyrazole-4-carboxylic acid (piperidin-4-ylmethyl)-amide



4-{[(1H-Pyrazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester (**EXAMPLE 34**) (600mg, 1.75mmol), 10% palladium on Carbon (150mg) and ethanol (15mL) were combined in a Parr® jar and hydrogenated at 50psi for 24h. The reaction mixture was filtered through Celite® and the filtrate was evaporated in vacuo to give the product as a white foam.

Step 2

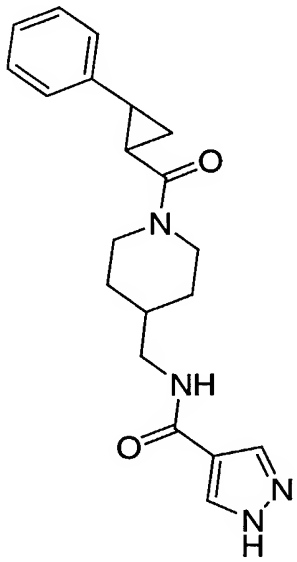
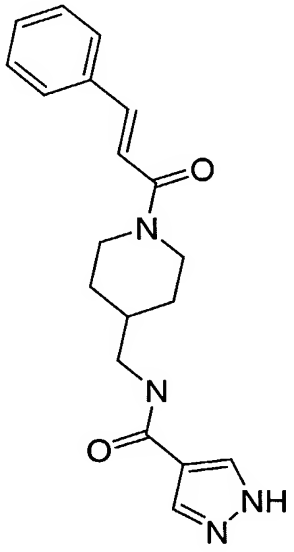
1H-Pyrazole-4-carboxylic acid [1-(3-phenyl-propionyl)-piperidin-4-ylmethyl]-amide



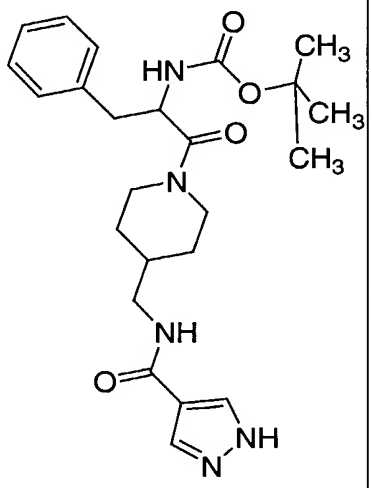
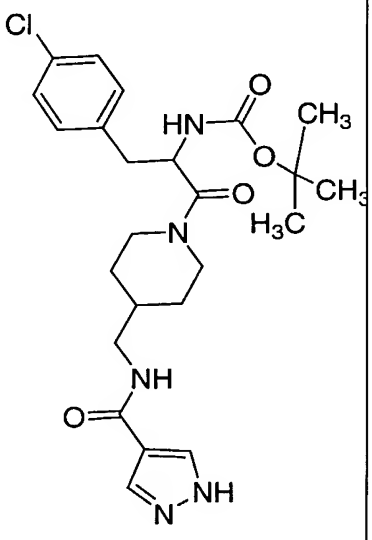
1H-Pyrazole-4-carboxylic acid (piperidin-4-ylmethyl)-amide (352mg, 1.69mmol), hydrocinnamoyl chloride (503 μL, 3.38mmol), diisopropylethylamine (294 μL, 1.69mmol) and DMF (4mL) were combined under Nitrogen and stirred at 25 °C for 24h. Sodium hydroxide (1mL, 2N) was added and the mixture was stirred 1h. Water was added and the contents of the reaction flask were extracted with EtOAc (3×50mL). The combined organic extracts were dried with Na_2SO_4 and filtered. The filtrate was removed in vacuo and the remaining residue was purified using an ISCO® normal phase silica chromatography system (CH_2Cl_2 (100%) to CH_2Cl_2:MeOH:NH_4OH 90:10:1). Fractions containing the desired product were combined and the solvent was removed in vacuo to give a colorless oil. Addition of EtOAc followed by 1N HCl/Et_2O gave the product as a white solid.

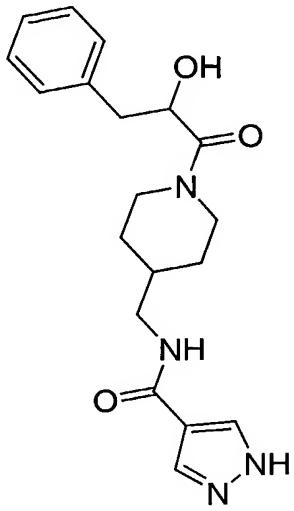
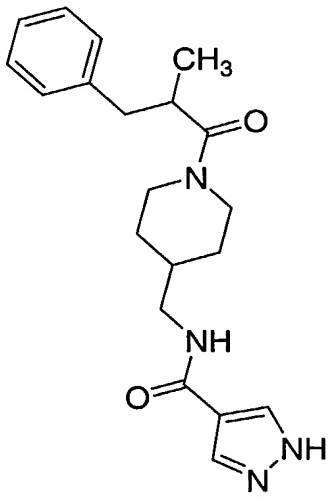
^{1}H NMR (500MHz, δ, DMSO-d_6): 8.10 (m, 1H), 8.04 (s, 2H), 7.28-7.20 (m, 4H), 7.18-7.14 (m, 1H), 4.38 (m, 1H), 3.85 (m, 1H), 3.06 (m, 2H), 2.90 (m, 1H), 2.80 (t, 2H), 2,60 (m, 2H), 1.75-1.60 (m, 4H), 0.95 (m, 2H).

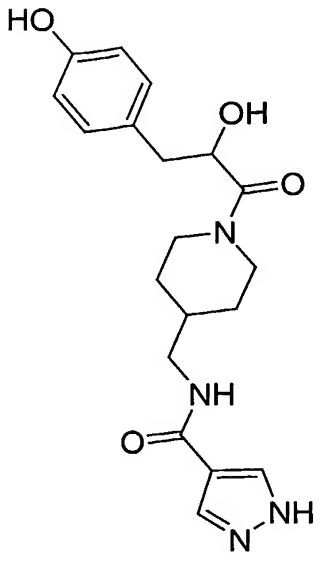
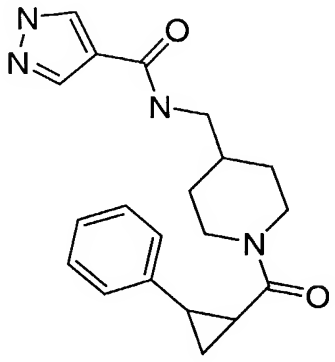
The following compounds were prepared by substituting the appropriate acid chloride for the hydrocinnamoyl chloride in the above procedure.

EX.	Name	Structure	Analytical Data
138	**1H-Pyrazole-4-carboxylic acid [1-(2-phenyl-cyclopropanecarbonyl)-piperidin-4-ylmethyl]-amide**		^{1}H NMR (500MHz, δ, DMSO-d_6): 8.08-7.98 (m, 3H), 7.26 (m, 2H), 7.17 (m, 3H), 4.38 (m, 1H), 4.16 (m, 1H), 3.15-2.97 (m, 3H), 2.58 (m, 1H), 2.26 (m, 2H), 1.80-1.60 (m, 3H), 1.30 (m, 1H), 1.20-0.95 (m, 3H).
139	**1H-Pyrazole-4-carboxylic acid [1-(3-phenyl-acryloyl)-piperidin-4-ylmethyl]-amide**		^{1}H NMR (500MHz, δ, DMSO-d_6): 8.16 (s, br, 1H), 8.07 (m, 1H), 7.88(s, br, 1H), 7.70 (m, 2H), 7.48-7.34 (m, 4H), 7.26 (m, 2H), 4.48 (m, 1H), 4.29 (m, 1H), 3.17-3.00 (m, 3H), 2.65 (m, 1H), 1.85-1.69 (m, 3H), 1.15-1.00 (m, 2H).

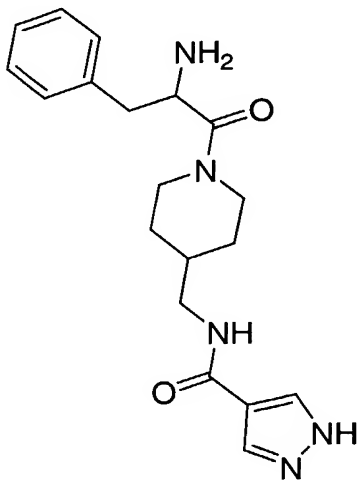
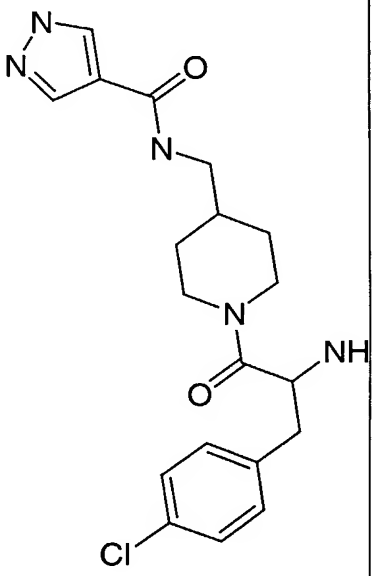
The following examples were prepared from 1H-pyrazole-4-carboxylic acid (piperidin-4-ylmethyl)-amide as described in **Example 1 Step 2.**

EX.	Name	Structure	Analytical Data
140	[1-Benzyl-2-oxo-2-(4-{[(1H-pyrazole-4-carbonyl)-amino]-methyl}-piperidin-1-yl)-ethyl]-carbamic acid tert-butyl ester		M.S. (M^++1) 456
141	[1-(4-Chloro-benzyl)-2-oxo-2-(4-{[(1H-pyrazole-4-carbonyl)-amino]-methyl}-piperidin-1-yl)-ethyl]-carbamic acid tert-butyl ester		M.S. (M^++1) 490

EX.	Name	Structure	Analytical Data
142	**1H-Pyrazole-4-carboxylic acid [1-(2-hydroxy-3-phenyl-propionyl)-piperidin-4-ylmethyl]-amide**		M.S. (M^++1) 357
143	**1H-Pyrazole-4-carboxylic acid [1-(2-methyl-3-phenyl-propionyl)-piperidin-4-ylmethyl]-amide**		M.S. (M^++1) 355

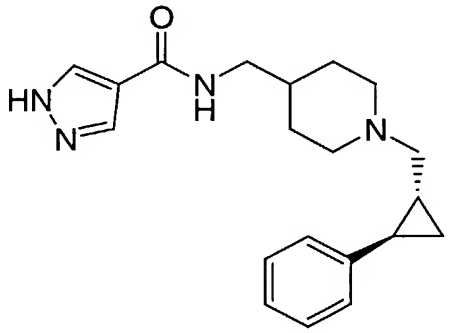
EX.	Name	Structure	Analytical Data
144	**1H-Pyrazole-4-carboxylic acid {1-[2-hydroxy-3-(4-hydroxy-phenyl)-propionyl]-piperidin-4-ylmethyl}-amide**		M.S. (M^++1) 373
145	**1H-Pyrazole-4-carboxylic acid [1-(2-phenyl-cyclopropanecarbonyl)-piperidin-4-ylmethyl]-amide**		M.S. (M^++1) 353

The following two compounds were prepared from **EXAMPLES 140** and **141** respectively by treatment with trifluoroacetic acid in dichloromethane.

EX.	Name	Structure	Analytical Data
146	1H-Pyrazole-4-carboxylic acid [1-(2-amino-3-phenyl-propionyl)-piperidin-4-ylmethyl]-amide		M.S. (M^++1) 356
147	1H-Pyrazole-4-carboxylic acid {1-[2-amino-3-(4-chloro-phenyl)-propionyl]-piperidin-4-ylmethyl}-amide		M.S. (M^++1) 390

EXAMPLE 148

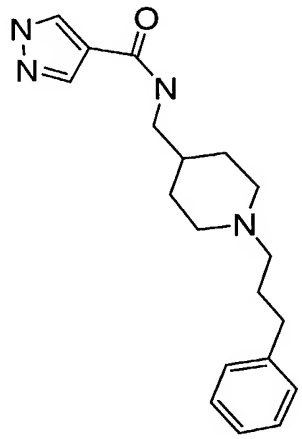
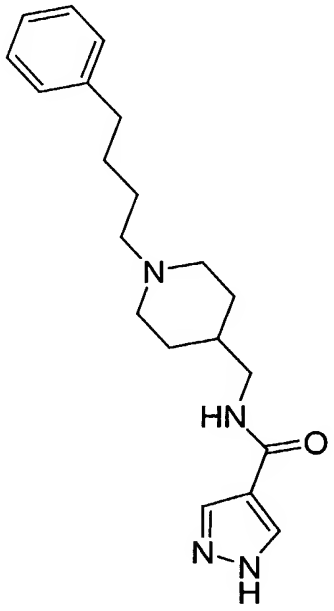
Trans 1H-Pyrazole-4-carboxylic acid [1-(2-phenyl-cyclopropylmethyl)-piperidin-4-ylmethyl]-amide

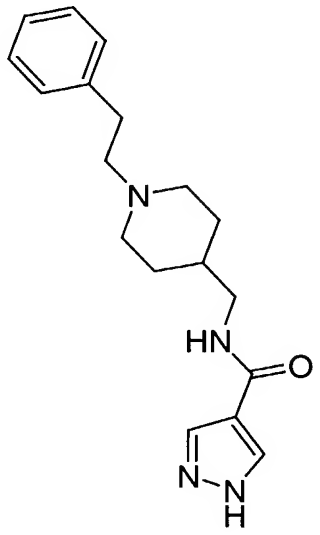
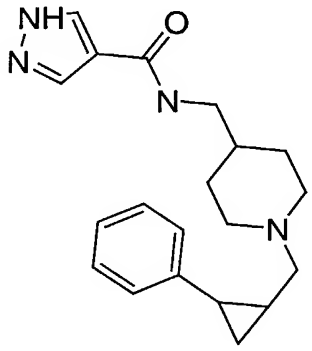


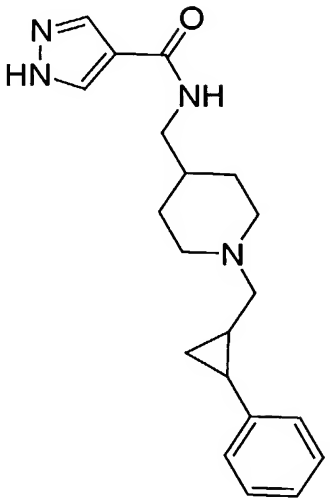
A solution of 1H-pyrazole-4-carboxylic acid (piperidin-4-ylmethyl)-amide (290mg, 1.39mmol), trans-2-phenylcyclopropanecarbaldehyde (224mg, 1.53mmol) and sodium triacetoxyborohydride (590mg, 2.78mmol) in MeOH (15mL) was heated to 50°C and stirred for 1h. The resulting reaction mixture was concentrated and purified by silica gel chromatography (gradient: CH_2Cl_2 to 80:20:2 CH_2Cl_2:MeOH:NH4OH) to give the trans 1H-pyrazole-4-carboxylic acid [1-(2-phenyl-cyclopropylmethyl)-piperidin-4-ylmethyl]-amide product.

^{1}H NMR (δ, $CDCl_3$): 7.86 (s, 2H), 7.23 (d, 2H), 7.17 (t, 1H), 7.02 (d, 2H), 5.94 (brt, 1H), 3.35 (m, 2H), 3.10 (brt, 2H), 2.55 (dd, 1H), 2.39 (dd, 1H), 2.03 (q, 2H), 1.70-1.55 (m, 4H), 1.41 (m, 2H), 1.22 (m, 1H), 0.95 (m, 1H), 0.82 (m, 1H).

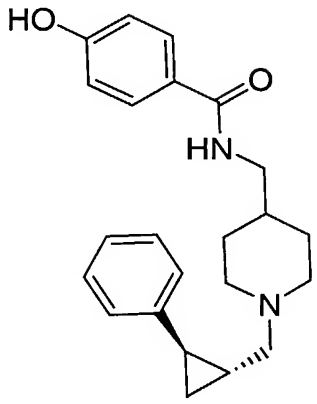
The following compounds were prepared similarly to the procedure described above for **EXAMPLE 148** but substituting the appropriate aldehyde for the trans-2-phenylcyclopropanecarbaldehyde.

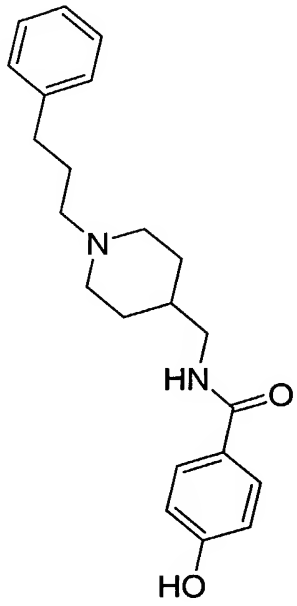
EX.	Name	Structure	Analytical Data
149	**1H-Pyrazole-4-carboxylic acid [1-(3-phenyl-propyl)-piperidin-4-ylmethyl]-amide**		^{1}H NMR (δ, $CDCl_3$): 7.93 (s, 2H), 7.3-7.15 (m, 5 H), 6.30 (brt, 1H), 3.35 (t, 2H), 3.04 (brd, 2H), 2.61 (t, 2H), 2.46 (dd, 2H), 2.04 (t, 2 H), 1.88 (m, 2H), 1.70 (m, 2H), 1.47 (m, 2 H), 1.27 (t, 1H).
150	**1H-Pyrazole-4-carboxylic acid [1-(4-phenyl-butyl)-piperidin-4-ylmethyl]-amide**		^{1}H NMR (δ, CD_3OD): 8.03 (s, 2H), 7.3-7.1 (m, 5H), 3.21 (d, 2H), 2.97 (brd, 2H), 2.63 (t, 2H), 2.40 (dd, 2H), 2.01 (t, 2 H), 1.76 (brd, 2H), 1.7-1.5 (m, 5H), 1.30 (m, 2H).

EX.	Name	Structure	Analytical Data
151	**1H-Pyrazole-4-carboxylic acid (1-phenethyl-piperidin-4-ylmethyl)-amide**		M.S. (M^++1) 313
152	**1H-Pyrazole-4-carboxylic acid [1-(2-phenyl-cyclopropylmethyl)-piperidin-4-ylmethyl]-amide**		M.S. (M^++1) 339

EX.	Name	Structure	Analytical Data
153	**1H-Pyrazole-4-carboxylic acid [1-(2-phenyl-cyclopropylmethyl)-piperidin-4-ylmethyl]-amide**		^{1}H NMR (δ, $CDCl_3$): 7.86 (s, 2H), 7.23 (d, 2H), 7.17 (t, 1H), 7.00 (d, 2H), 6.61 (brs, 1H), 3.30 (m, 2H), 3.10 (brt, 2H), 2.55 (dd, 1H), 2.39 (dd, 1H), 2.03 (q, 2H), 1.70-1.55 (m, 4H), 1.41 (m, 2H), 1.22 (m, 1H), 0.95 (m, 1H), 0.82 (m, 1H).

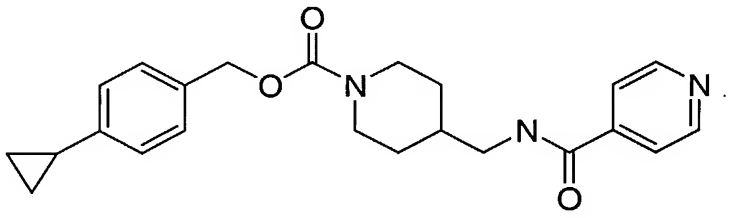
The following compounds were prepared as described above for **EXAMPLE 148**, but replacing 1H-pyrazole-4-carboxylic acid (piperidin-4-ylmethyl)-amide with, for example, 4-hydroxy-N-piperidin-4-ylmethyl-benzamide, which was prepared from 4-[(4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester as described in **EXAMPLE 137, step 1**.

EX.	Name	Structure	Analytical Data
154	**4-Hydroxy-N-[1-(2-phenyl-cyclopropylmethyl)-piperidin-4-ylmethyl]-benzamide**		^{1}H NMR (δ, $CDCl_3$): 7.43 (d, 2H), 7.3-7.1 (m, 3H), 7.00 (d, 2H), 6.65 (d, 2H), 6.39 (brt, 1H), 3.35 (m, 2H), 3.14 (brt, 2H), 2.58 (dd, 1H), 2.41 (dd, 1H), 2.08 (q, 2H), 1.7-1.5 (m, 4H), 1.41 (m, 2H), 1.22 (m, 1H), 0.96 (m, 1H), 0.82 (m, 1H).

EX.	Name	Structure	Analytical Data
155	**4-Hydroxy-N-[1-(3-phenyl-propyl)-piperidin-4-ylmethyl]-benzamide**		^{1}H NMR (δ, CD_3OD): 7.70 (d, 2H), 7.3-7.1 (m, 5H), 6.80 (d, 2H), 3.23 (d, 2H), 3.02 (brd, 2H), 2.61 (dd, 2H), 2.42 (dd, 2H), 2.08 (brt, 2H), 1.9-1.6 (m, 5H), 1.35 (m, 2H).

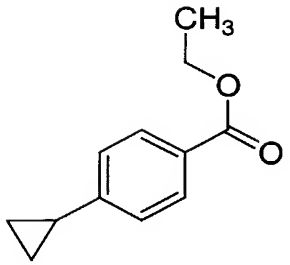
EXAMPLE 156:

4-{[(Pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-cyclopropyl-benzyl ester



Step 1:

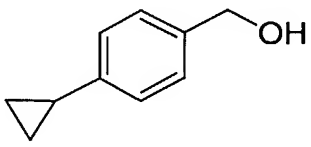
4-Cyclopropyl-benzoic acid ethyl ester



Indium trichloride (2.2g, 10mmol) and THF (50mL) were combined under nitrogen and cooled to -70°C. Cyclopropylmagnesium bromide solution (33mL, 30mmol, 0.92M) was added dropwise while maintaining the reaction temperature ≤-60°C. After the addition was complete the reaction was stirred 0.5h with cooling then 0.5h with the cooling bath removed. The resulting solution was added via cannula to a refluxing solution of ethyl-4-iodobenzoate (5.5g, 20mmol), *trans*-dichlorobis(triphenylphosphine)palladium(II) (421mg, 0.60mmol) and THF (100mL) under nitrogen. After 24h, the contents of the reaction flask were cooled and the solvent was removed *in vacuo*. Water (100mL) and 5% $KHSO_4$ were added and the mixture was extracted with CH_2Cl_2 (3×100mL). The combined organic extracts were washed with brine, dried with Na_2SO_4 and filtered. The filtrate was removed *in vacuo* and the remaining residue was purified by flash column chromatography (hexane:EtOAc 95:5) to give the 4-cyclopropyl-benzoic acid ethyl ester as an orange oil.

Step 2

(4-Cyclopropyl-phenyl)-methanol

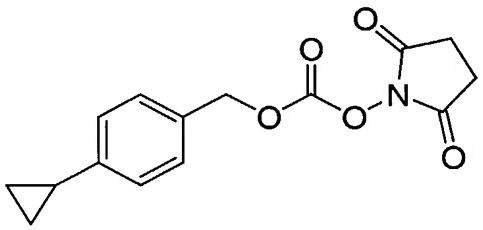


4-Cyclopropyl-benzoic acid ethyl ester (2.46g, 13mmol), and THF (250mL) were combined under nitrogen and cooled in an IPA/dry ice bath to -70°C. Lithium aluminum hydride solution (20mL, 20mmol, 1.0M) was added dropwise. After 2h excess lithium aluminum hydride was quenched by adding EtOAc dropwise. The reaction was warmed to 25°C then the solvent was removed *in vacuo*. Water (200mL) and a few drops of HCl(aq, 6N) were added. The mixture was extracted

with EtOAc (3×100mL). The combined organic extracts were washed with brine, dried with Na_2SO_4 and filtered. The filtrate was removed *in vacuo* and the remaining residue was purified by flash column chromatography (hexane:EtOAc 40:60) to give the (4-cyclopropyl-phenyl)-methanol as a colorless oil.

Step 3

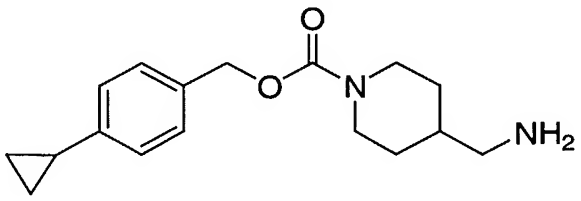
Carbonic acid 4-cyclopropyl-benzyl ester 2,5-dioxo-pyrrolidin-1-yl ester



The title compound was prepared from (4-Cyclopropyl-phenyl)-methanol as described above for similar compounds (*Chem..Pharm. Bull.*, 38(1):110-115(1990)).

Step 4

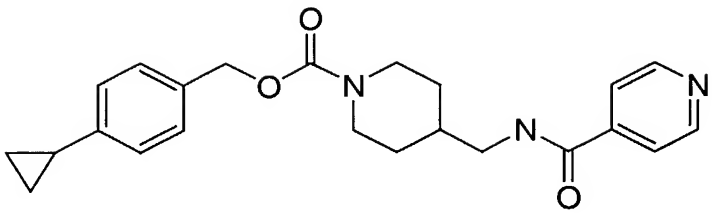
4-Aminomethyl-piperidine-1-carboxylic acid 4-cyclopropyl-benzyl ester



The title compound was prepared from carbonic acid 4-cyclopropyl-benzyl ester 2,5-dioxo-pyrrolidin-1-yl ester as described in **EXAMPLE 1, Step 1.**

Step 5

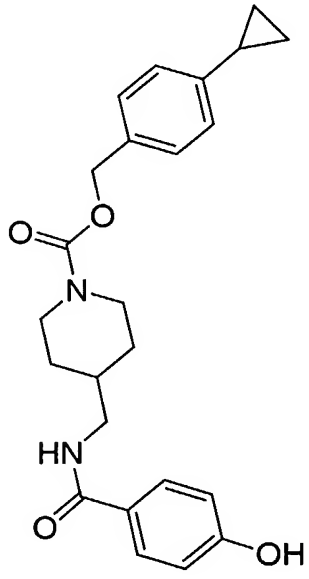
4-{[(Pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-cyclopropyl-benzyl ester

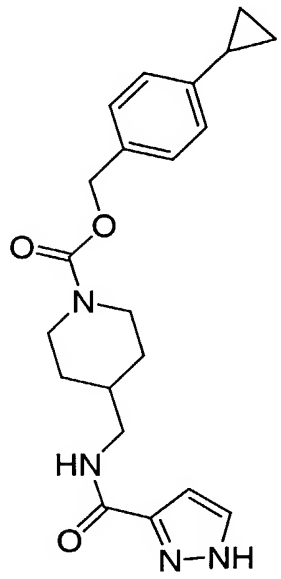
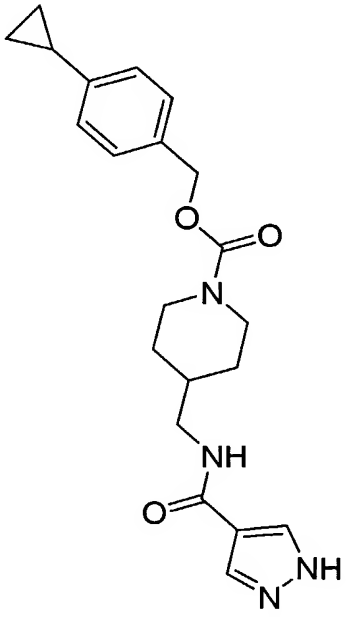


The title compound was prepared from 4-aminomethyl-piperidine-1-carboxylic acid 4-cyclopropyl-benzyl ester as described above in **EXAMPLE 1, Step 2.**

M.S. (M^++1) 394

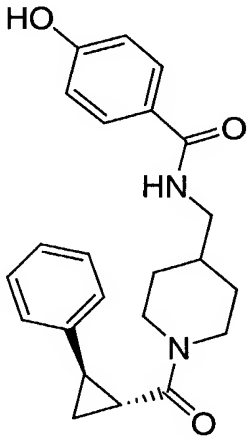
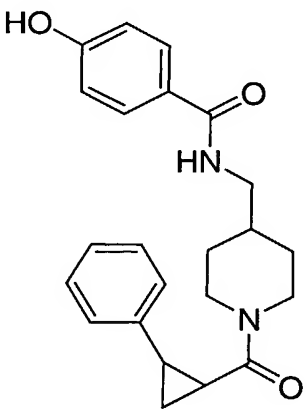
The following compounds were prepared from 4-aminomethyl-piperidine-1-carboxylic acid 4-cyclopropyl-benzyl ester as described above in **EXAMPLE 1, step 2.**

EX.	Name	Structure	Analytical Data
157	**4-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid 4-cyclopropyl-benzyl ester**		M.S. (M^++1) 409

EX.	Name	Structure	Analytical Data
158	**4-{[(1H-Pyrazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-cyclopropyl-benzyl ester**		M.S. (M^++1) 383
159	**4-{[(1H-Pyrazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-cyclopropyl-benzyl ester**		^{1}H NMR (500MHz δ, $CDCl_3$): 10.70 (s, br, 1H), 7.95 (s, 2H), 7.25 (d, 2H), 7.05 (d, 2H), 6.00 (m, 1H), 5.06 (s, 2H), 4.20 (s, br, 2H), 3,30 (s, br, 2H),.2.75 (s, br, 2H), 1.90 (m, 1H), 1.85-1.50 (m, 3H), 1.20 (m, 2H), 0.97 (m, 2H), 0.68 (m, 2H).

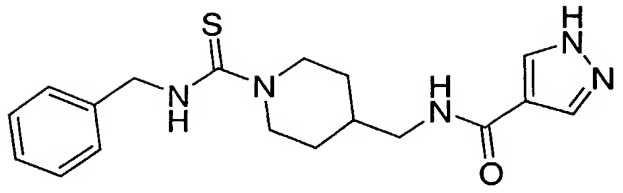
The following compounds were prepared from 4-hydroxy-N-piperidin-4-ylmethyl-benzamide (prepared from 4-[(4-hydroxy-benzoylamino)-methyl]-

piperidine-1-carboxylic acid benzyl ester as described in **EXAMPLE 137, step 1**) as described in **EXAMPLE 1, Step 2**.

EX.	Name	Structure	Analytical Data
160	**4-Hydroxy-N-[1-(2-phenyl-cyclopropanecarbonyl)-piperidin-4-ylmethyl]-benzamide**		^{1}H NMR (δ, $CDCl_3$): 8.72 (brs, 1H), 7.61 (d, 2H), 7.24 (m, 2H), 7.19 (t, 1H), 7.06 (d, 2H), 6.93 (d, 2H), 6.72 (brs, 1H), 4.55 (brd, 1H), 4.10 (brd, 1H), 3.3-3.1 (m, 2H), 3.01 (q, 1H), 2.58 (brt, 1H), 2.41 (brs, 1H), 2.0-1.6 (m, 5H), 1.3-1.1 (m, 3H).
161	**4-Hydroxy-N-[1-(2-phenyl-cyclopropanecarbonyl)-piperidin-4-ylmethyl]-benzamide**		M.S. (M^++1) 379

EXAMPLE 162:

1H-Pyrazole-4-carboxylic acid (1-benzylthiocarbamoyl-piperidin-4-ylmethyl)-amide

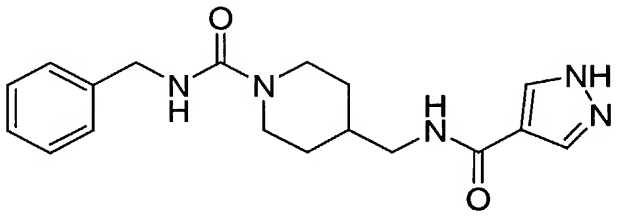


1H-Pyrazole-4-carboxylic acid (piperidin-4-ylmethyl)-amide **(EXAMPLE 137, Step 1)** (50mg, 0.24mmol), benzyl isothiocyanate (35μL, 0.264mmol) and DMF (1mL) were combined and stirred under Nitrogen for 1h. The contents of the reaction flask were poured into water and sodium hydroxide (2mL, 2N) was added. The resulting mixture was extracted with EtOAc (3×50mL) and the combined organic extracts were dried with Na_2SO_4. The filtrate was removed in vacuo and the remaining residue was purified by Gilson® reverse phase preparative HPLC. The fraction containing the desired product was evaporated in vacuo to give a colorless oil. Trituration with EtOAc/EtOH afforded the **EXAMPLE 162** as a white solid.

^{1}H NMR (500MHz, δ, DMSO-d_6): 13.10 (s, 1H), 8.20 (m, 2H), 8.10 (m, 1H), 7.90 (m, 1H), 7.32-7.18 (m, 5H), 4.80 (d, 2H), 4.65 (d, 2H), 3.10 (t, 2H), 2.97 (t, 2H), 1.80 (m, 1H), 1.67 (m, 2H), 1.10 (m, 2H).

EXAMPLE 163:

4-{[(1H-Pyrazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzylamide

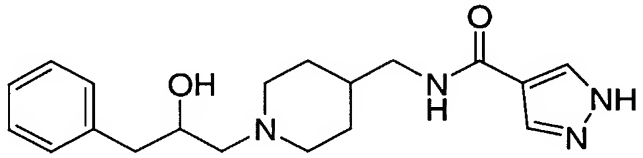


The title compound was prepared as described in **EXAMPLE 162** except that benzyl isocyanate was used instead of benzyl isothiocyanate.

^{1}H NMR (500MHz, δ, DMSO-d_6): 13.10 (s, 1H), 8.16 (s, 1H), 8.04 (m, 1H), 7.88 (s, 1H), 7.30-7.16 (m, 4H), 7.02 (m, 1H), 4.21 (d, 2H), 3.99 (d, 2H), 3.10 (t, 2H), 2.65 (m, 2H), 1.72-1.58 (m, 3H), 1.05-0.95 (m, 2H).

EXAMPLE 164:

1H-Pyrazole-4-carboxylic acid [1-(2-hydroxy-3-phenyl-propyl)-piperidin-4-ylmethyl]-amide

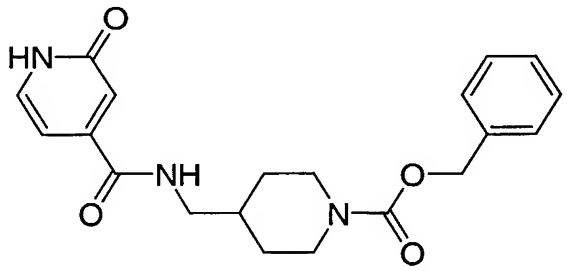


To a solution of 2-benzyloxirane (0.01mL, 0.07mmol) in iso-propyl alcohol (5mL) was added 1H-pyrazole-4-carboxylic acid (piperidin-4-ylmethyl)-amide (**EXAMPLE 137, Step 1**) (15mg, 0.07mmol). The resulting reaction mixture was heated to 60°C for 24h. The reaction mixture was concentrated, partitioned between EtOAc and aqueous sodium bicarbonate. The organic phase was dried, the solvent evaporated, and the crude product purified by reverse phase HPLC to give 1H-Pyrazole-4-carboxylic acid [1-(2-hydroxy-3-phenyl-propyl)-piperidin-4-ylmethyl]-amide.

M.S. (M^++1) 343

EXAMPLE 165:

4-{[(2-Oxo-1,2-dihydro-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester



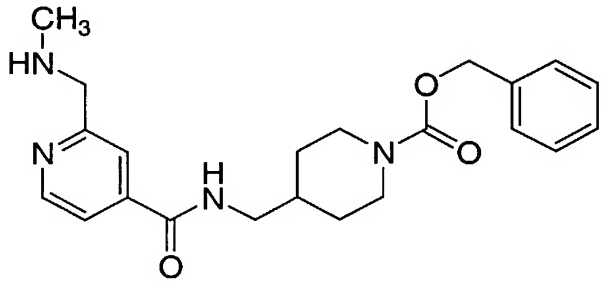
To 4-{[(1-oxy-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester (**EXAMPLE 115**) (200mg, 0.542mmol) was added acetic anhydride (5mL) and the mixture heated to reflux for 24h. The reaction was concentrated and chromatographed on silica using ethyl acetate to give an oil (40mg). The crude material was dissolved in methanol (10mL) and treated with solid

potassium carbonate (40mg) for 0.5h. Concentration of the reaction and extraction into dichloromethane (20mL) from aqueous sodium bicarbonate (20mL) followed by concentration and precipitation of the solid from ether gave the 4-{[(2-Oxo-1,2-dihydro-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester.

M.S.(M+1): 370

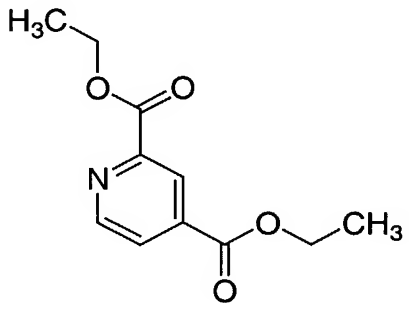
EXAMPLE 166:

4-{[(2-Methylaminomethyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester



Step 1:

Preparation of 2,4-pyridinedicarboxcyclic acid diethyl ester

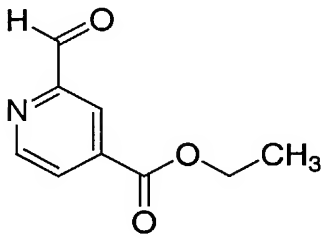


To a mixture of 2,4-pyridinedicarboxylic acid (23g, 0.138mol) in ethanol (500mL) was bubbled anhydrous hydrogen chloride gas over a period of 6h. The resulting reaction mixture was concentrated *in vacuo* and extracted into dichloromethane (500mL) from 10 % aqueous sodium bicarbonate (500mL). The organic extract was dried over sodium sulfate, and concentrated *in vacuo* to give 2,4-pyridinedicarboxcyclic acid diethyl ester as an oil.

M.S.(M+1): 224

Step 2:

Preparation of 2-Formyl-isonicotinic acid ethyl ester

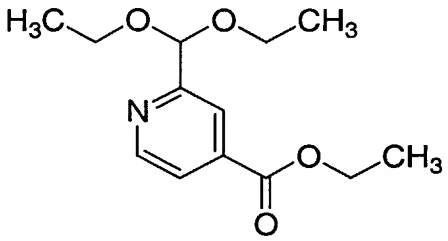


To a solution of 2,4-pyridinedicarboxcyclic acid diethyl ester (25g, 0.112mol) in tetrahydrofuran (1L) at –78°C and under nitrogen was slowly added a solution of 1.0M diisobutylaluminum hydride in THF (11mL). The reaction was stirred at –78°C for 5h and then quenched by addition of a solution of tetrahydrofuran-acetic acid-water (174mL, 62mL, 15mL) and the reaction allowed to warm to room temperature. Diethyl ether (500mL) and 10% aqueous sodium bicarbonate (1L) were added and the mixture stirred for 0.5h. The ether layer was removed and the aqueous layer extracted with ethyl acetate (4X500mL) The combined organic extracts were washed with saturated sodium chloride and concentrated to an oil which was purified by silica gel column chromatography using 30 %ethyl acetate/hexane as eluent to give 2-formyl-isonicotinic acid ethyl ester as an oil.

M.S.(M+1): 180

Step 3:

Preparation of 2-Diethoxymethyl-isonicotinic acid ethyl ester

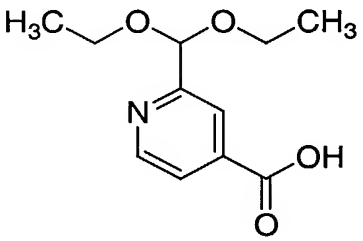


To a solution of 2-formyl-isonicotinic acid ethyl ester (5.0g, 0.027mol) in ethanol (9mL) was added triethyl orthoformate (6.2mL, 0.037mol) followed by a solution of 6N hydrochloric acid in ethanol (1.5mL). The mixture was heated to 110°C (reflux) for 1.5h, cooled to rt and solid potassium carbonate (1.80g) added. The mixture was stirred for 5min, concentrated in vacuo, and redissolved in diethyl ether (100mL). The reaction was filtered through silica and the resulting cake washed with diethyl ether (50mL). The filtrated was concentrated in vacuo to give 2-diethoxymethyl-isonicotinic acid ethyl ester as an oil.

M.S.(M+1): 254

Step 4:

Preparation of 2-Diethoxymethyl-isonicotinic acid

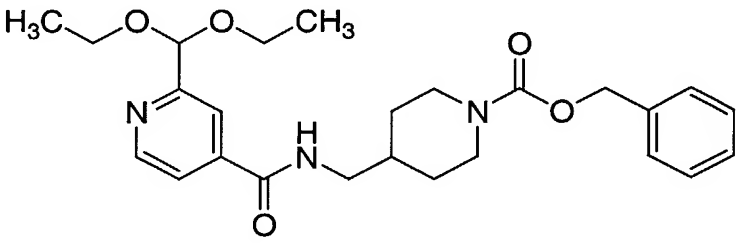


To a solution of 2-diethoxymethyl-isonicotinic acid ethyl ester (3.0g, 0.012mol) in tetrahydrofuran (100mL) was added 1N sodium hydroxide (24mL, 0.024mol) and mixture allowed to stir for 2h at rt. The reaction was concentrated in vacuo to give a pasty solid of 2-diethoxymethyl-isonicotinic acid, which was used in the next step as is.

M.S.(M+1): 226

Step 5:

Preparation of 4-{[(2-Diethoxymethyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester

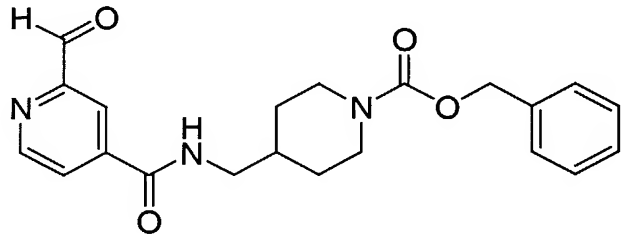


4-{[(2-Diethoxymethyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester was prepared in a similar manner as described in **EXAMPLE 1, Step 2.**

M.S.(M+1): 456

Step 6:

Preparation of 4-{[(2-Formyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester

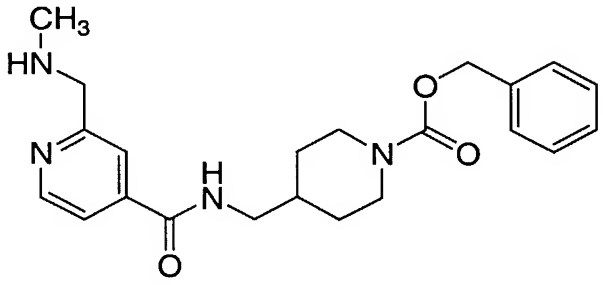


To a solution of 4-{[(2-diethoxymethyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester (1.3g, 0.0029mol) in dioxane (20mL) was added 1N hydrochloric acid (40mL) and the mixture was warmed to 50°C for 1.5h. The reaction was cooled, diluted with ethyl acetate (100mL) and 10 % aqueous sodium bicarbonate (100mL), and stirred well. The organic layer was removed, dried over sodium sulfate, filtered and concentrated *in vacuo* to give 4-{[(2-formyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester as an oil.

M.S.(M+1): 382

Step 7:

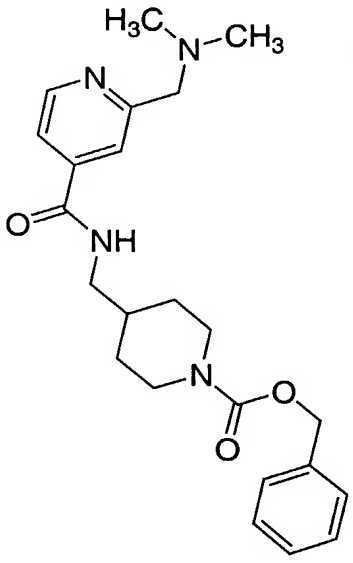
Prep of 4-{[(2-Methylaminomethyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester

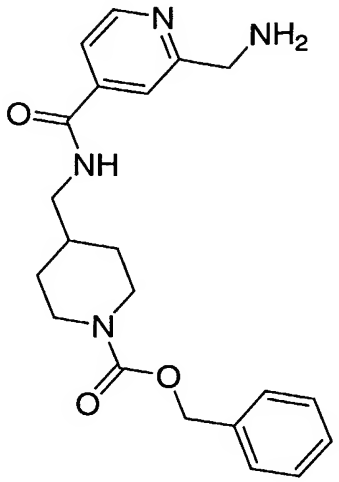


To a solution of 4-{[(2-formyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester (50mg, 0.13mmol) in dichloroethane (0.5mL) was added acetic acid (8μL, 0.13mmol), 2.0M methylamine in THF (72μL, 0.14mmol) followed by sodium triacetoxyborohydride (42mg, 0.20mmol). The resulting mixture was stirred for 5h. The reaction was concentrated *in vacuo* and the residue chromatographed (reverse phase C-18 using acetonitrile/0.1 % trifluoroacetic acid in water) to give upon concentration *in vacuo* 4-{[(2-methylaminomethyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester as the trifluoroacetic acid salt.

M.S. (M^++1) 397

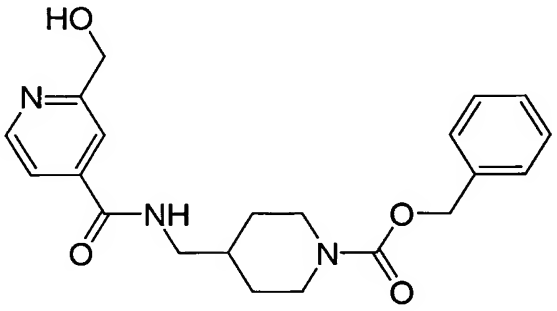
The following compounds were prepared as described above for 4-{[(2-methylaminomethyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester, replacing methylamine with the appropriate amine in **step 7, EXAMPLE 166.**

EX.	Name	Structure	Analytical Data
167	**4-{[(2-Dimethylaminomethyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 411

168	**4-{[(2-Aminomethyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		M.S. (M^++1) 383

EXAMPLE 169:

4-{[(2-Hydroxymethyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester

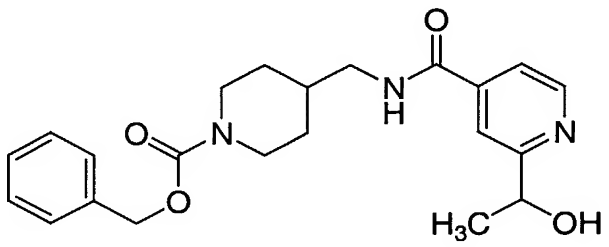


To a solution of 4-{[(2-formyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester (**EXAMPLE 166, Step 6**) (50mg, 0.131mmol) in ethanol (2mL) was added sodium borohydride (5mg) and the mixture stirred for 0.5h. The reaction was diluted with 10% aqueous sodium bicarbonate (10mL) and extracted with ethyl acetate (25mL). The ethyl acetate extract was concentrated and chromatographed (reverse phase C-18 using acetonitrile/0.1 % trifluoroacetic acid in water) to give upon concentration *in vacuo* the 4-{[(2-hydroxymethyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester as the trifluoroacetic acid salt.

M.S.(M+1): 384

EXAMPLE 170:

4-({[2-(1-Hydroxy-ethyl)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid benzyl ester

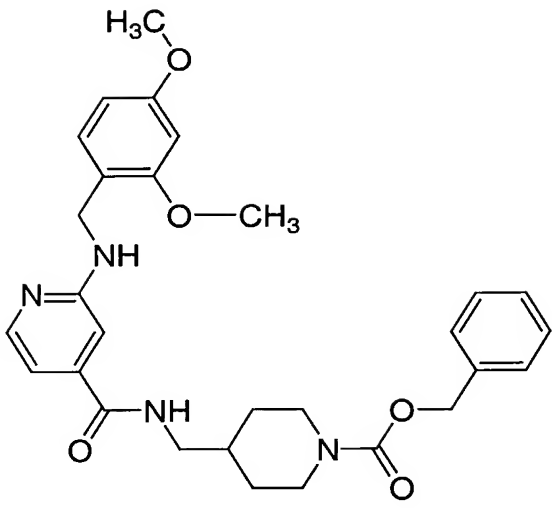


To a solution of 4-{[(2-formyl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester (**EXAMPLE 166, Step 6**) (50mg, 0.131mmol) in THF (2mL) at –78°C was added 3.0M methylmagnesium chloride (45μL, 0.135mmol). The mixture was stirred for 5min and allowed to warm to rt. The reaction was diluted with 10% aqueous sodium bicarbonate (10mL) and extracted with ethyl acetate (25mL). The ethyl acetate extract was concentrated and chromatographed on silica using 100% ethyl acetate to ethyl acetate/methanol (95/5) to give the 4-({[2-(1-hydroxy-ethyl)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid benzyl ester.

M.S. (M^++1) 398

EXAMPLE 171:

4-({[2-(2,4-Dimethoxy-benzylamino)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid benzyl ester

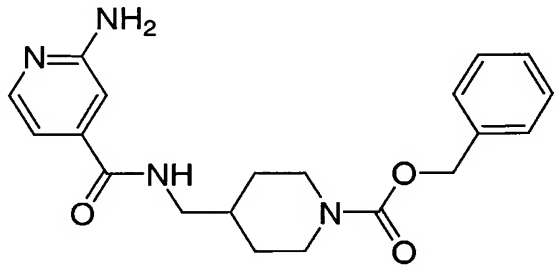


A mixture of 4-{[(2-chloro-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester (**EXAMPLE 65**) (310mg, 0.8mmol) and 2,4-dimethoxybenzylamine (1mL) were heated to 140°C for 18h, cooled to rt, and partitioned between pH5.2 citrate buffer and EtOAc. The organic layer was dried and the solvent evaporated to give the crude product, purified by chromatography on silica (1:1 hexane EtOAc to 5% MeOH EtOAc to give the 4-({[2-(2,4-Dimethoxy-benzylamino)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid benzyl ester.

M.S. (M^++1) 519

EXAMPLE 172:

4-{[(2-Amino-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester

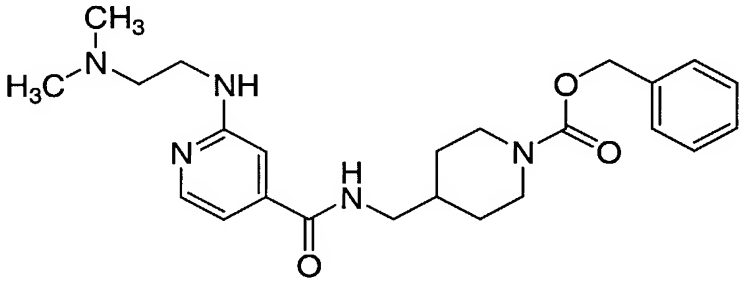


4-({[2-(2,4-Dimethoxy-benzylamino)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid benzyl ester (**EXAMPLE 171**) (124mg) in dichloromethane (5mL) was treated with trifluoroacetic acid (0.5mL). After 30min, the reaction mixture was partitioned between EtOAc and dilute sodium bicarbonate solution. The organic layer was washed with brine, dried and the solvent evaporated to give the crude product which was stirred with ether (3mL) and filtered to give the 4-{[(2-amino-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester as a white solid.

M.S. (M^++1) 369

EXAMPLE 173:

4-({[2-(2-Dimethylamino-ethylamino)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid benzyl ester

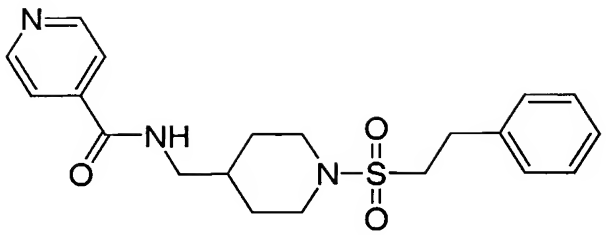


A mixture of 4-{[(2-chloro-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester (**EXAMPLE 65**) (50mg, 0.8mmol) and N,N-dimethylethylenediamine (0.2mL) were heated to 100C for 18 hours, cooled to room temperature. The reaction mixture was then purified by reverse phase HPLC to give the 4-({[2-(2-dimethylamino-ethylamino)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid benzyl ester as its trifluoroacetate salt.

M.S. (M^++1) 440

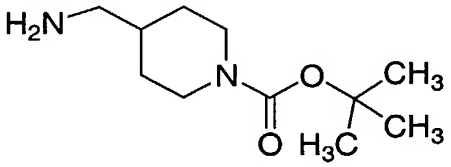
EXAMPLE 174:

N-[1-(2-Phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-isonicotinamide



Step 1:

4-Aminomethyl-piperidine-1-carboxylic acid tert-butyl ester

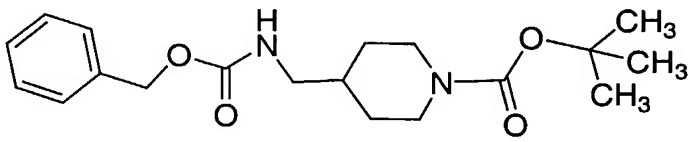


To a mixture of 15g of 4-aminomethylpiperidine in 250mL of anhydrous tetrahydrofuran cooled to –78°C was added dropwise over 45min a solution of 24g of di-tert-butyl di-carbonate in 100mL of anhydrous tetrahydrofuran. After stirring for 1h at –78°C, the mixture was allowed to warm to rt and stirred overnight. The mixture was concentrated to near dryness and diluted with 200mL of 10% aqueous citric acid. The mixture was extracted with 3x100mL of ether, then made basic with sodium hydroxide pellets and extracted with 3x200mL of chloroform. The combined chloroform extracts were dried over magnesium sulfate and concentrated to dryness under reduced pressure. The resulting oil was homogeneous by TLC (development with 90:10 chloroform saturated with ammonia: methanol).

^{1}H NMR (400MHz, $CDCl_3$): 4.1 (br s, 2 H), 2.7 (br m, 2H), 2.6 (d, 2H), 1.7 (m, 3H), 1.42 (s, 9H), 1.1 (m, 2H).

Step 2:

4-(Benzyloxycarbonylamino-methyl)-piperidine-1-carboxylic acid tert-butyl ester

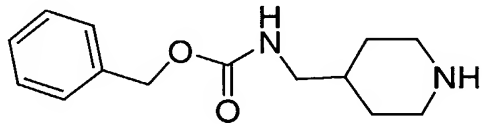


To a solution of 21g of 4-aminomethyl-piperidine-1-carboxylic acid tert-butyl ester in 100mL of ethyl acetate cooled to 0°C was added 100mL of saturated sodium carbonate and 17g of benzyl chloroformate. The solution was stirred for 3h, then separated. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure. Drying under vacuum gave the product as an oil:

^{1}H NMR (400MHz, $CDCl_3$): 7.35 (m, 5H), 5.3 (d, 1H), 5.1 (s, 2H), 4.1 (br s, 2 H), 3.0 (br m, 2H), 2.6 (br m, 2H), 1.7 (m, 3H), 1.42 (s, 9H), 1.1 (m, 2H).

Step 3:

Piperidin-4-ylmethyl-carbamic acid benzyl ester



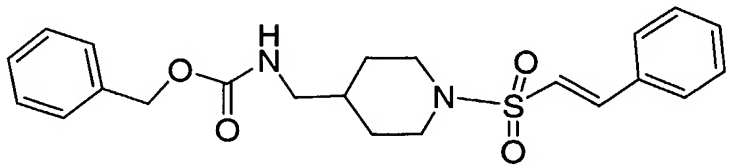
A mixture of 35g of 4-(benzyloxycarbonylamino-methyl)-piperidine-1-carboxylic acid tert-butyl ester and 50mL of 4N HCl in dioxane was stirred at rt for 3h, then diluted with 200mL of ether and filtered. The piperidin-4-ylmethyl-carbamic acid benzyl ester hydrochloride salt was obtained as a white fluffy solid. The free base was obtained by partitioning the hydrochloride between 50mL chloroform and 50mL saturated aqueous Na_2CO_3.

MS (m+1) = 249;

^{1}H NMR (400MHz, $CDCl_3$)): 7.35 (m, 5H), 5.15 (s, 2H), 4.9 (br s, 1 H), 3.1 (m, 2H), 2.6 (m, 3H), 1.7 (m, 2H), 1.6 (m, 2H), 1.1 (m, 2H).

Step 4:

[1-(2-Phenyl-ethenesulfonyl)-piperidin-4-ylmethyl]-carbamic acid benzyl ester



A mixture of 2g of piperidin-4-ylmethyl-carbamic acid benzyl ester hydrochloride, 25mL of dichloromethane, 1.5 grams of trans-2-styrenesulfonyl chloride, and 3mL of N,N-diisopropylethylamine was stirred at rt overnight, then

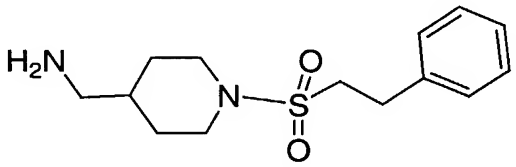
diluted with 200mL of chloroform, and washed with 100mL of saturated sodium carbonate. The chloroform extracts were dried over magnesium sulfate and concentrated. The [1-(2-phenyl-ethenesulfonyl)-piperidin-4-ylmethyl]-carbamic acid benzyl ester was obtained as a white solid.

MS (m+1) = 415;

^{1}H NMR (400MHz, $CDCl_3$)): 7.5-7.2 (m, 10H), 6.65 (m, 1H), 5.15 (s, 2H), 4.8 (br s, 1 H), 3.8 (d, 2H), 3.1 (dd, 2H), 2.6 (dd, 2H), 1.8 (d, 2H), 1.6 (m, 2H), 1.35 (m, 2H).

Step 5:

C-[1-(2-Phenyl-ethanesulfonyl)-piperidin-4-yl]-methylamine



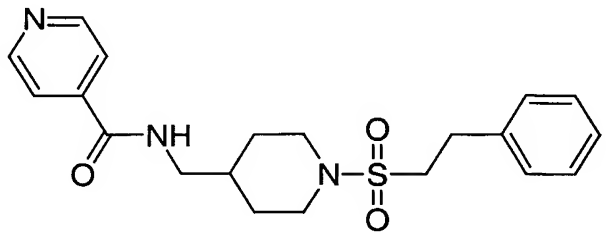
A mixture of 2.5g of [1-(2-phenyl-ethenesulfonyl)-piperidin-4-ylmethyl]-carbamic acid benzyl ester, 1g of 20% palladium hydroxide on carbon, 200mL of methanol and 50mL of tetrahydrofuran were shaken under 50psi of hydrogen for 2 days at rt. The catalyst was filtered off and washed with 250mL of methanol. Concentration under reduced pressure gave the C-[1-(2-phenyl-ethanesulfonyl)-piperidin-4-yl]-methylamine as a white solid.

MS (m+1) = 283;

^{1}H NMR (400MHz, $CDCl_3$)): 7.4-7.2 (m, 5H), 5.1 (s, 2H), 3.8 (d, 2H), 3.1 (m, 4H), 2.7 (dd, 2H), 1.8 (d, 2H), 1.6 (m, 5H), 1.3 (m, 2H).

Step 6:

N-[1-(2-Phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-isonicotinamide

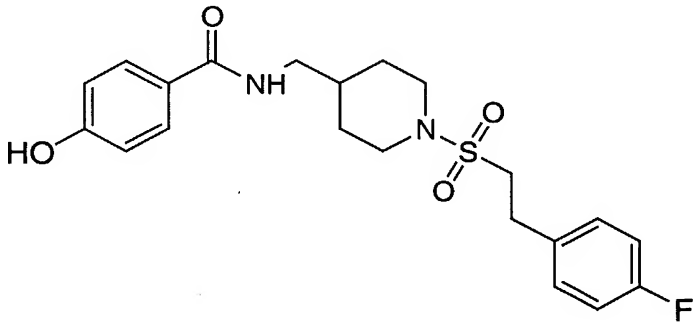


The N-[1-(2-Phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-isonicotinamide was prepared from C-[1-(2-phenyl-ethanesulfonyl)-piperidin-4-yl]-methylamine and isonicotinic acid as described above in **EXAMPLE 1, Step 2.**

MS (m+1) = 388.

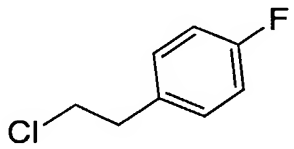
EXAMPLE 175:

N-{1-[2-(4-Fluoro-phenyl)-ethanesulfonyl]-piperidin-4-ylmethyl}-4-hydroxy-benzamide



Step 1:

1-(2-Chloro-ethyl)-4-fluoro-benzene

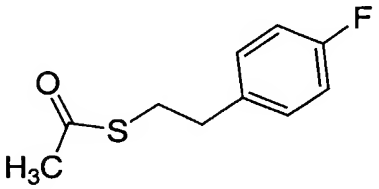


A mixture of 7g of 2-(4-fluoro-phenyl)-ethanol, 25mL of chlorobenzene, 42mL of 37% HCl, and 0.9g of Aliquat® 336 (tricaprylylmethyl ammonium chloride) was heated to reflux for 3 days, cooled and extracted into 3x100mL of hexane. The combined extracts were dried over magnesium sulfate and concentrated under reduced pressure. The resulting oil was a crude product of 1-(2-chloro-ethyl)-4-fluoro-benzene:

^{1}H NMR (400MHz, $CDCl_3$): 7.3 (dd, 2H), 7.0 (dd, 2H), 3.7 (t, 2H), 3.05 (t, 2H).

Step 2:

Thioacetic acid S-[2-(4-fluoro-phenyl)-ethyl] ester

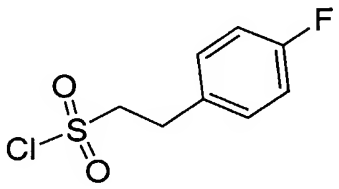


A mixture of 2.4g of 1-(2-chloro-ethyl)-4-fluoro-benzene, 30mL of DMF, and 2.5g of potassium thioacetate was stirred under nitrogen for 24h. The mixture was diluted with 200mL of water and extracted with 3X50mL of dichloromethane. The combined organic layers were dried over magnesium sulfate and concentrated under reduced pressure. Drying under vacuum gave the product as an oil:

^{1}H NMR (400MHz, $CDCl_3$): 7.18 (dd, 2H), 6.98 (dd, 2H), 3.08 (t, 2H), 2.81 (t, 2H), 2.32 (s, 3H).

Step 3:

2-(4-Fluoro-phenyl)-ethanesulfonyl chloride

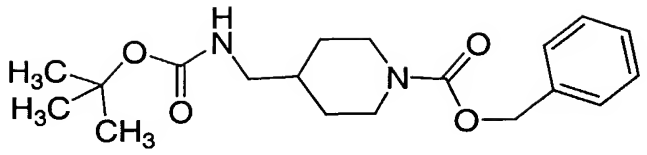


A stream of chlorine gas was dispersed into a stirred, ice cold mixture of 2.5g of thioacetic acid S-[2-(4-fluoro-phenyl)-ethyl] ester, 30mL of dichloromethane and 30mL of water over 1h. The mixture was diluted with 200mL of dichloromethane, shaken and separated. The combined organic layers were dried over magnesium sulfate and concentrated under reduced pressure. Trituration with hexane gave a white solid:

^{1}H NMR (400MHz, $CDCl_3$): 7.2 (dd, 2H), 7.0 (dd, 2H), 3.1 (dd, 2H), 3.3 (dd, 2H), 2.32 (s, 3H).

Step 4:

4-(tert-Butoxycarbonylamino-methyl)-piperidine-1-carboxylic acid benzyl ester

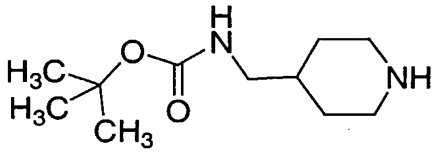


To an ice cold, stirred solution of 21g of 4-aminomethyl-piperidine-1-carboxylic acid benzyl ester in 250mL of dichloromethane was added 18g of di-tert-butyldicarbonate in 100mL of dichloromethane over 30min. After stirring overnight, the mixture was concentrated to dryness. Trituration with hexane gave a white solid:

^{1}H NMR (400MHz, $CDCl_3$): 7.4 (m, 5H), 5.15 (s, 2H), 4.6 (br s, 1H), 4.2 (br s, 2H), 3.0 (br s, 2H), 2.8 ((m, 2H), 1.7 (m, 3H), 1.42 (s, 9H), 1.15 (m, 2H).

Step 5:

Piperidin-4-ylmethyl-carbamic acid tert-butyl ester

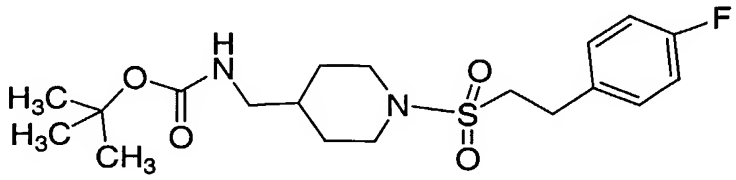


A mixture of 28g of 4-(tert-butoxycarbonylamino-methyl)-piperidine-1-carboxylic acid benzyl ester, 1g of 10% palladium on carbon, 100mL of THF and 200mL of methanol was stirred under an atmosphere of hydrogen for 2 days. The mixture was filtered concentrated under reduced pressure. Drying under reduced pressure gave a white solid:

^{1}H NMR (400MHz, $CDCl_3$): 4.8 (br s, 1H), 3.05 (d, 2H), 2.9 (dd, 2H), 2.6 (m, 3H), 1.6 (d, 2H), 1.5 (m, 1H), 1.4 (s, 9H), 1.05 (m, 2H).

Step 6:

{1-[2-(4-Fluoro-phenyl)-ethanesulfonyl]-piperidin-4-ylmethyl}-carbamic acid tert-butyl ester

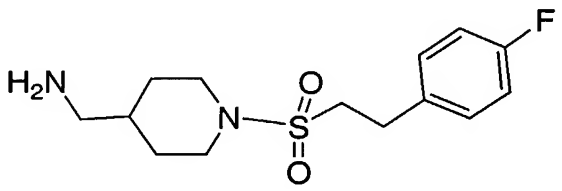


To an ice cold, stirred solution of 0.2g of piperidin-4-ylmethyl-carbamic acid tert-butyl ester and 0.2mL of N,N-diisopropylethyl amine in 20mL of dichloromethane was added 0.3g of 2-(4-fluoro-phenyl)-ethanesulfonyl chloride. After stirring overnight, the mixture was diluted with 50mL of chloroform, washed with 50mL of saturated sodium carbonate, dried over magnesium sulfate and concentrated to dryness under reduced pressure. Trituration with hexane gave a white solid:

^{1}H NMR (400MHz, $CDCl_3$): 7.2 (m, 2H), 7.0 (dd, 2H), 4.6 (br m, 1H), 3.8 (d, 2H), 3.1 (m, 3H), 3.0 (m, 2H), 2.7 (dd, 2H), 1.8 (d, 2H), 1.6 (br m, 2H), 1.42 (s, 9H), 1.3 (m, 2H).

Step 7:

C-{1-[2-(4-Fluoro-phenyl)-ethanesulfonyl]-piperidin-4-yl}-methylamine



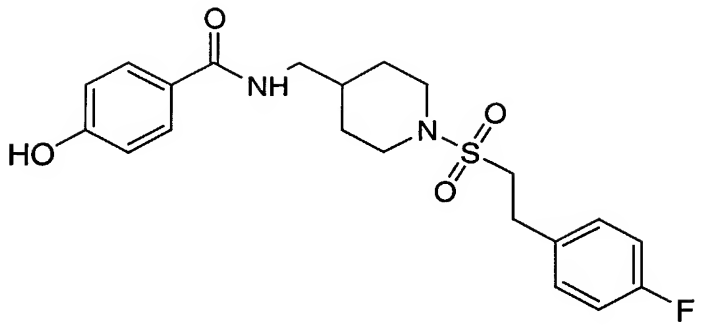
A mixture of 0.4g of {1-[2-(4-fluoro-phenyl)-ethanesulfonyl]-piperidin-4-ylmethyl}-carbamic acid tert-butyl ester and 5mL of 4N HCl in dioxane was stirred at rt for 3h, then diluted with 50mL of chloroform, washed with 50mL of saturated sodium carbonate, dried over magnesium sulfate and concentrated to dryness under reduced pressure. The product was a white solid:

MS (m+1) = 301;

^{1}H NMR (400MHz, $CDCl_3$): 7.2 (m, 2H), 7.0 (dd, 2H), 3.92 (d, 2H), 3.1 (s, 4H), 2.7 (dd, 2H), 2.6 (d, 2H), 1.8 (d, 2H), 1.5 (br m, 3H), 1.3 (m, 2H).

Step 8

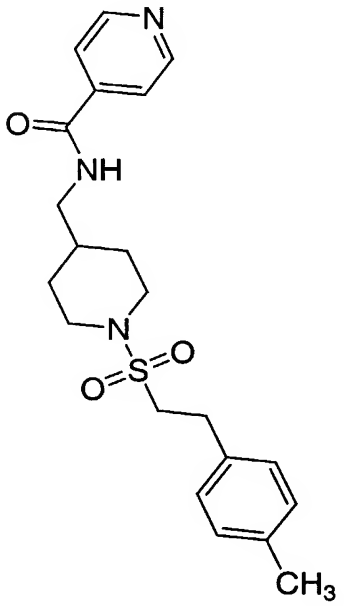
N-{1-[2-(4-Fluoro-phenyl)-ethanesulfonyl]-piperidin-4-ylmethyl}-4-hydroxy-benzamide

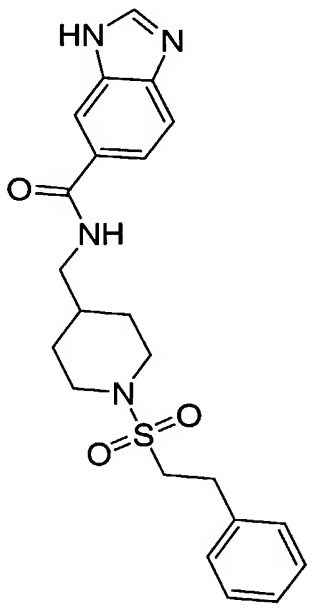
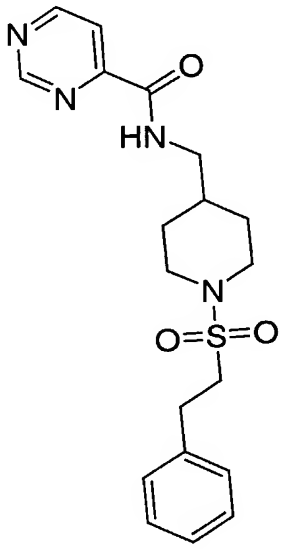


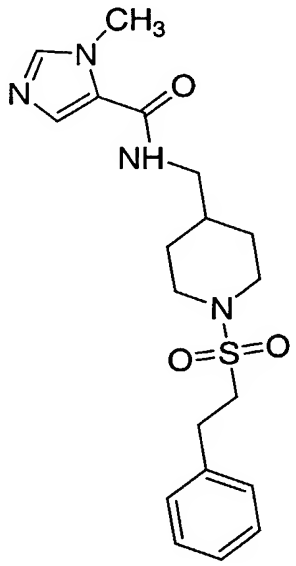
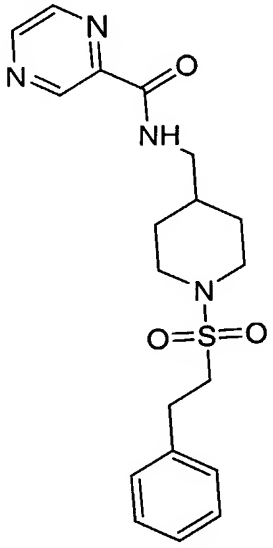
N-{1-[2-(4-Fluoro-phenyl)-ethanesulfonyl]-piperidin-4-ylmethyl}-4-hydroxy-benzamide was prepared from C-{1-[2-(4-fluoro-phenyl)-ethanesulfonyl]-piperidin-4-yl}-methylamine and 4-hydroxybenzoic acid as described above in **EXAMPLE 1, Step 2.**

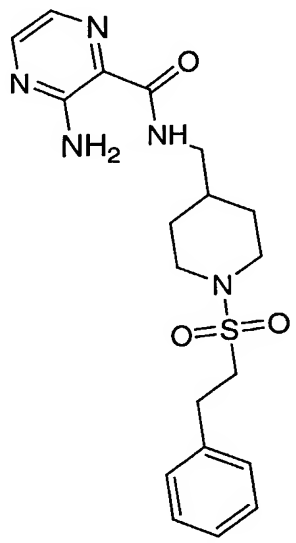
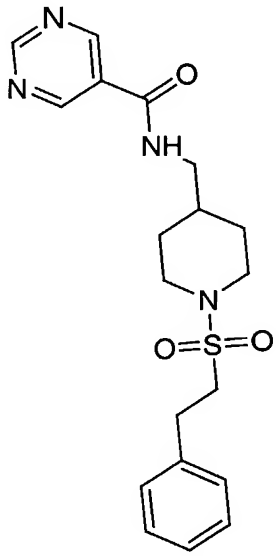
MS (m+1) = 421.

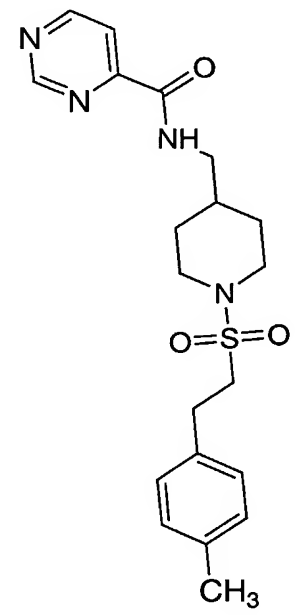
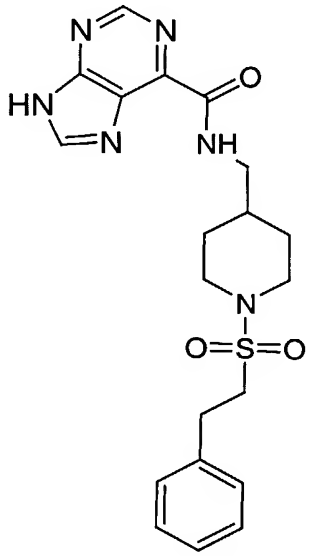
The following compounds were prepared as described in **EXAMPLE 175**, but replacing the 4-fluorophenethyl alcohol with the appropriately substituted phenethyl alcohol in **Step 1** and using the appropriate carboxylic acid in **Step 8.**

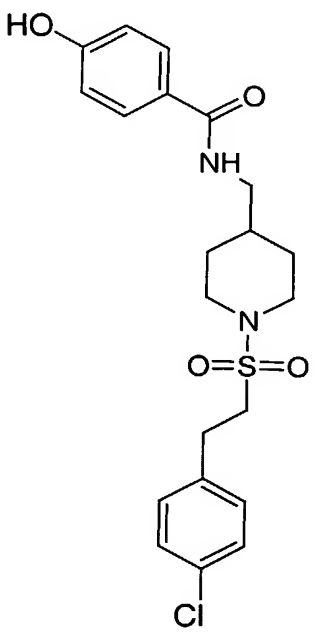
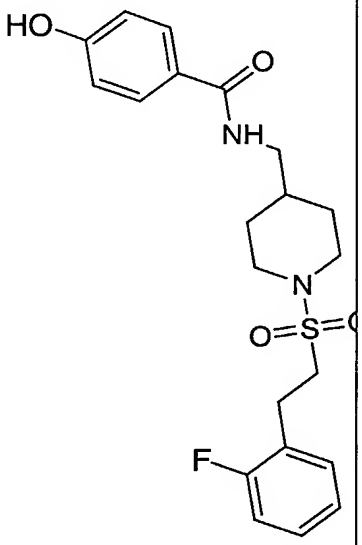
EX.	Name	Structure	Analytical Data
176	**N-[1-(2-p-Tolyl-ethanesulfonyl)-piperidin-4-ylmethyl]-isonicotinamide**		MS (m+1) = 402.5.

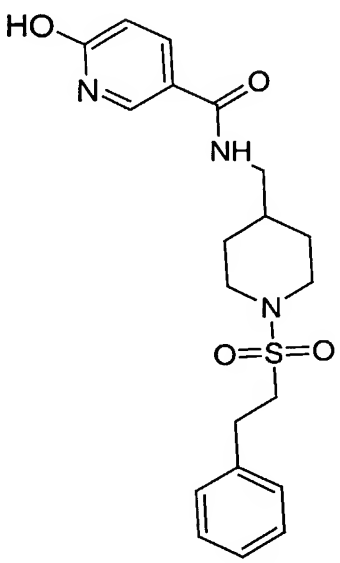
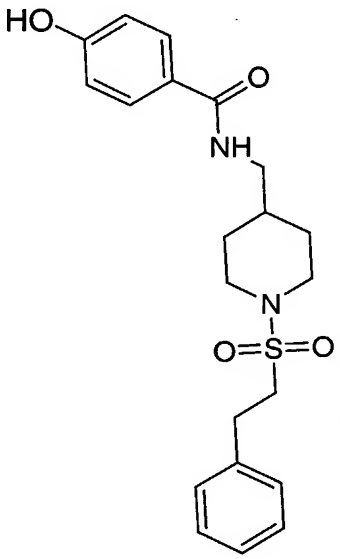
EX.	Name	Structure	Analytical Data
177	**3H-Benzoimidazole-5-carboxylic acid [1-(2-phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-amide**		MS (m+1) = 427.5.
178	**Pyrimidine-4-carboxylic acid [1-(2-phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-amide**		MS (m+1) = 389.

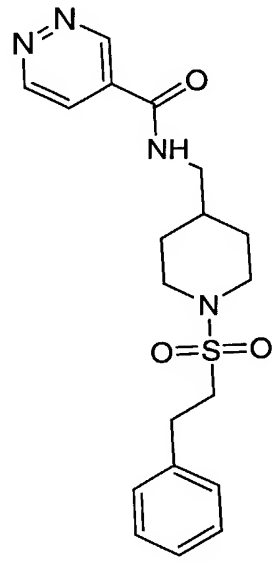
EX.	Name	Structure	Analytical Data
179	**2-Amino-pyrimidine-5-carboxylic acid [1-(2-phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-amide**		MS (m+1) = 391
180	**Pyrazine-2-carboxylic acid [1-(2-phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-amide**		MS (m+1) = 389

EX.	Name	Structure	Analytical Data
181	**3-Amino-pyrazine-2-carboxylic acid [1-(2-phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-amide**		MS (m+1) = 404
182	**Pyrimidine-5-carboxylic acid [1-(2-phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-amide**		MS (m+1) = 389

EX.	Name	Structure	Analytical Data
183	**Pyrimidine-4-carboxylic acid [1-(2-p-tolyl-ethanesulfonyl)-piperidin-4-ylmethyl]-amide**		MS (m+1) = 389
184	**9H-Purine-6-carboxylic acid [1-(2-phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-amide**		MS (m+1) = 429

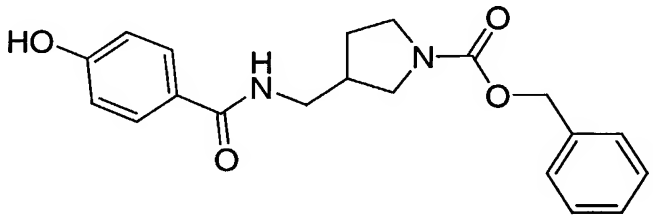
EX.	Name	Structure	Analytical Data
185	**N-{1-[2-(4-Chloro-phenyl)-ethanesulfonyl]-piperidin-4-ylmethyl}-4-hydroxy-benzamide**		MS (m+1) = 437
186	**N-{1-[2-(2-Fluoro-phenyl)-ethanesulfonyl]-piperidin-4-ylmethyl}-4-hydroxy-benzamide**		MS (m+1) = 421

EX.	Name	Structure	Analytical Data
187	**6-Hydroxy-N-[1-(2-phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-nicotinamide**		MS (m+1) = 404
188	**4-Hydroxy-N-[1-(2-phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-benzamide**		MS (m+1) = 403

EX.	Name	Structure	Analytical Data
189	**Pyridazine-4-carboxylic acid [1-(2-phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-amide**		MS (m+1) = 389

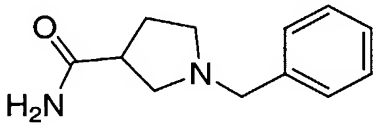
EXAMPLE 190:

(R,S) 3-[(4-Hydroxy-benzoylamino)-methyl]-pyrrolidine-1-carboxylic acid benzyl ester



Step 1:

1-Benzyl-pyrrolidine-3-carboxylic acid amide

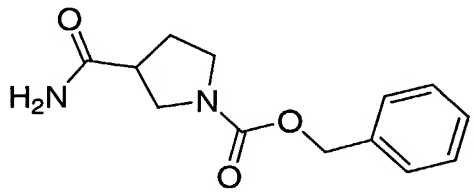


To a mixture of 4.4g of 1-benzyl-pyrrolidine-3-carboxylic acid methyl ester (M. J. Kornet et al., *J. Org. Chem.*, **33**:3637-3639(**1968**)) and 3g of formamide in 10mL of anhydrous DMF heated to 100°C was added a solution of sodium methoxide, from 0.33g of sodium dissolved in methanol, dropwise over 20min. After stirring for 1h at 100°C, the mixture was allowed to cool to rt and added to 100mL of isopropanol. The mixture was concentrated to dryness. The resulting residue was triturated with 200mL of chloroform, filtered and concentrated to dryness under reduced pressure. The resulting oil was fairly homogeneous by TLC (development with 90:10 chloroform saturated with ammonia: methanol):

^{1}H NMR (400MHz, $CDCl_3$): 7.1 (5H), 4.3 (br s, 2 H), 3.5 (d, 2H), 3.4 (m, 1H), 2.6 (m, 2H), 2.5 (m, 1H), 2.25 (m, 1H), 1.9 (m, 1H).

Step 2:

3-Carbamoyl-pyrrolidine-1-carboxylic acid benzyl ester

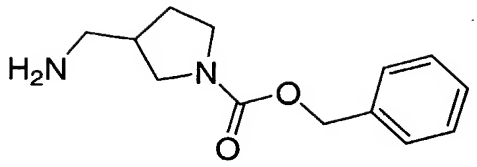


A mixture of 4.5g of 1-benzyl-pyrrolidine-3-carboxylic acid amide, 200mL of THF, 20mL of methanol, and 1g of 20% palladium hydroxide on carbon was shaken under 50psi of hydrogen for 12h. The catalyst was filtered off and the filtrate concentrated under reduced pressure. Drying under vacuum gave 3g of an oil. To a stirred solution of the crude residue in 500mL of chloroform was added 5.5g of N-(benzyloxycarbonyloxy)succinimide and 2.2mL of triethylamine. The mixture was allowed to stir overnight and washed with 50mL of saturated sodium carbonate dried over magnesium sulfate and concentrated to dryness. Purification by chromatography on silica gel, eluting with 90:10 ethyl acetate: methanol, gave the product as a resin:

^{1}H NMR (400MHz, $CDCl_3$): 7.35 (m, 5H), 5.6 (br m, 2H), 3.6 (m, 3H), 3.4 (m, 1H), 2.9 (br m, 1H), 2.1 (m, 2H).

Step 3:

3-Aminomethyl-pyrrolidine-1-carboxylic acid benzyl ester

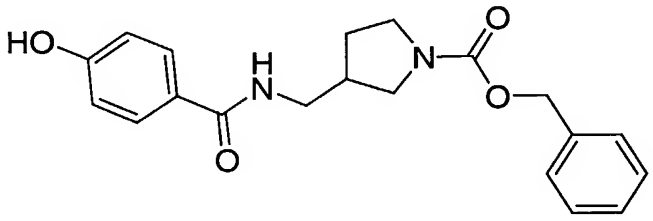


A mixture of 1g of 3-carbamoyl-pyrrolidine-1-carboxylic acid benzyl ester and 24mL of 1M borane-THF was stirred at room temperature for 24h, then quenched with 50mL of 3N HCl. The mixture was concentrated under reduced pressure, followed by being partitioned between 50mL chloroform and 25mL saturated aqueous sodium carbonate. Concentration of the combined extracts after drying over magnesium sulfate gave the product as a resin:

^{1}H NMR (400MHz, $CDCl_3$)): 7.35 (m, 5H), 5.15 (s, 2H), 3.7-4 (complex, 4H), 2.7 (m, 1H), 2.4-2.0 (complex, 2H), 1.6 (m, 4H).

Step 4:

(R,S) 3-[(4-Hydroxy-benzoylamino)-methyl]-pyrrolidine-1-carboxylic acid benzyl ester

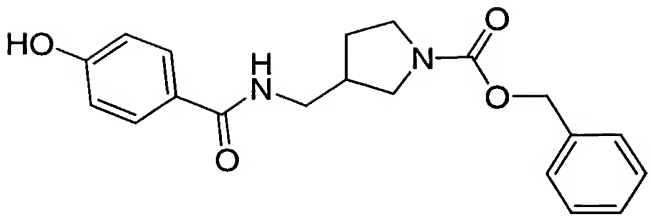


(R,S) 3-[(4-Hydroxy-benzoylamino)-methyl]-pyrrolidine-1-carboxylic acid benzyl ester was prepared from 3-aminomethyl-pyrrolidine-1-carboxylic acid benzyl ester and 4-hydroxybenzoic acid as described above in **EXAMPLE 1, Step 2.**

MS (m+1) = 395.

EXAMPLE 191:

(R) 3-[(4-Hydroxy-benzoylamino)-methyl]-pyrrolidine-1-carboxylic acid benzyl ester and (S) 3-[(4-Hydroxy-benzoylamino)-methyl]-pyrrolidine-1-carboxylic acid benzyl ester

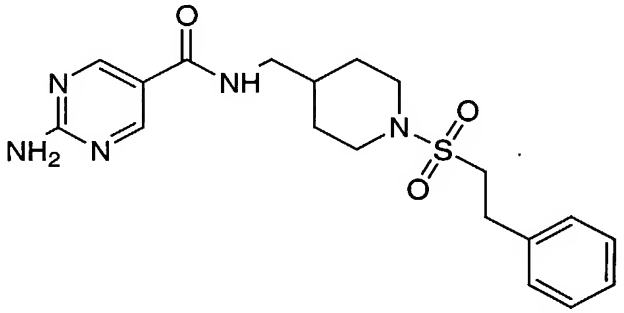


Resolution of (R,S) 3-[(4-hydroxy-benzoylamino)-methyl]-pyrrolidine-1-carboxylic acid benzyl ester (**EXAMPLE 190**) was performed on a Chirapak® preparative chiral HPLC column:

MS (m+1) = 395.

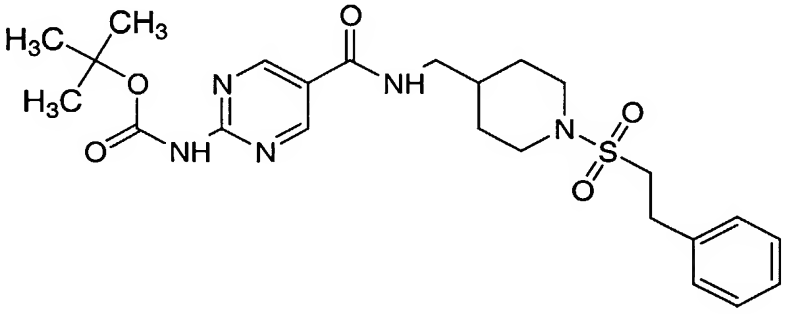
EXAMPLE 192:

2-Amino-pyrimidine-5-carboxylic acid [1-(2-phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-amide



Step 1:

(5-{[1-(2-Phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-carbamoyl}-pyrimidin-2-yl)-carbamic acid tert-butyl ester

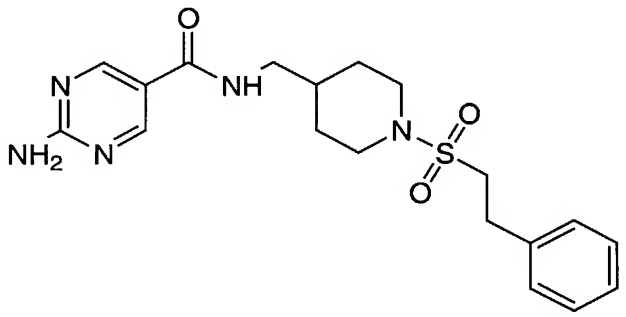


(5-{[1-(2-Phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-carbamoyl}-pyrimidin-2-yl)-carbamic acid tert-butyl ester was prepared from C-[1-(2-phenyl-ethanesulfonyl)-piperidin-4-yl]-methylamine and 2-tert-butoxycarbonylamino-pyrimidine-5-carboxylic acid (prepared by BOC protection of ethyl 2-amino-5-pyrimidine carboxylate [prepared as described by P. Schenone, et al., *J. Heterocyclic Chem.*, 27:295-305(1990)] using di-tert-butyl dicarbonate and 4-dimethylaminopyridine in acetonitrile, followed by saponification with sodium hydroxide and neutralization with dilute aqueous HCl) as described in **EXAMPLE 1, Step 2**:

MS (m+1) = 504.

Step 2:

2-Amino-pyrimidine-5-carboxylic acid [1-(2-phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-amide

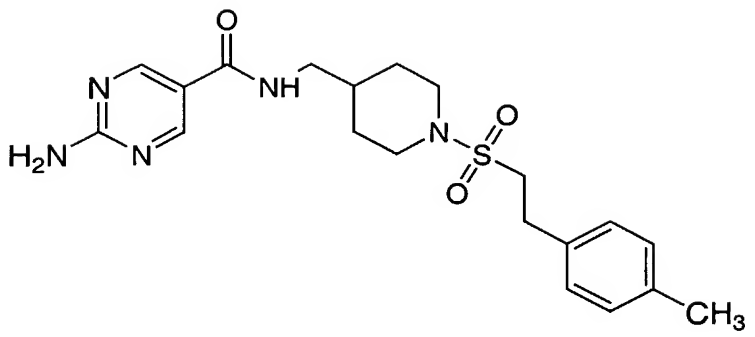


2-Amino-pyrimidine-5-carboxylic acid [1-(2-phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-amide was prepared from (5-{[1-(2-phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-carbamoyl}-pyrimidin-2-yl)-carbamic acid tert-butyl ester by stirring at rt for 3h in 4N HCl in dioxane. The product was precipitated as the hydrochloride salt by dilution with ether and filtration.

MS (m+1) = 404.

EXAMPLE 193:

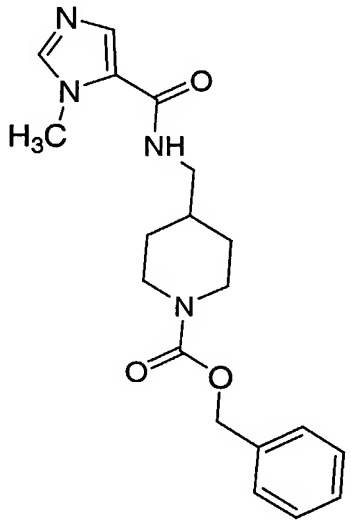
2-Amino-pyrimidine-5-carboxylic acid [1-(2-p-tolyl-ethanesulfonyl)-piperidin-4-ylmethyl]-amide

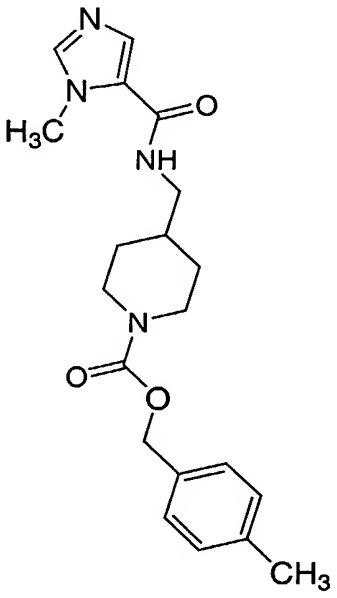
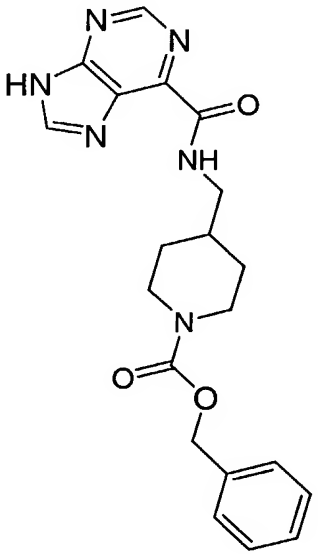


The title compound was prepared from C-[1-(2-p-tolyl-ethanesulfonyl)-piperidin-4-yl]-methylamine and 2-tert-butoxycarbonylamino-pyrimidine-5-carboxylic acid, followed by treatment with 4N HCl in dioxane as described in **EXAMPLE 192**.

MS (m+1) = 418.

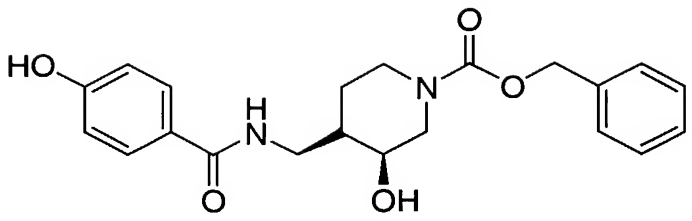
The following compounds were prepared by coupling 4-aminomethyl-piperidine-1-carboxylic acid benzyl ester (**EXAMPLE 1, Step 1**) with the appropriate acid as described in **EXAMPLE 1, Step 2**.

EX.	Name	Structure	Analytical Data
194	**4-{[(3-Methyl-3H-imidazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		MS (m+1) = 357

EX.	Name	Structure	Analytical Data
195	**4-{[(3-Methyl-3H-imidazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester**		MS (m+1) = 371
196	**4-{[(9H-Purine-6-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester**		MS (m+1) = 395

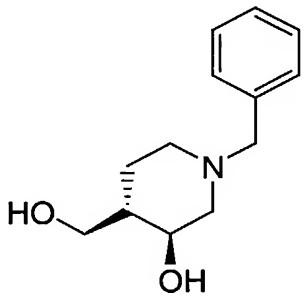
EXAMPLE 197:

3-Hydroxy-4-[(4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester



Step 1:

1-Benzyl-4-hydroxymethyl-piperidin-3-ol

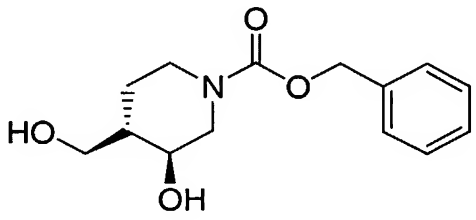


Sodium borohydride (40g) was added in portions to a stirred solution of ethyl N-benzyl-3-oxopiperidine-4-carboxylate hydrochloride in methanol (500mL), over 2h. Water (300mL) was added slowly, the mixture stirred for 15min, and then the organics were evaporated. The resulting residue was partitioned between DCM and water (x3), the combined organic layers dried over anhydrous sodium sulfate, and the solvent evaporated to give the product as a cis trans mixture, used in the next step without further purification.

M.S. (M+1): 222.

Step 2:

3-Hydroxy-4-hydroxymethyl-piperidine-1-carboxylic acid benzyl ester

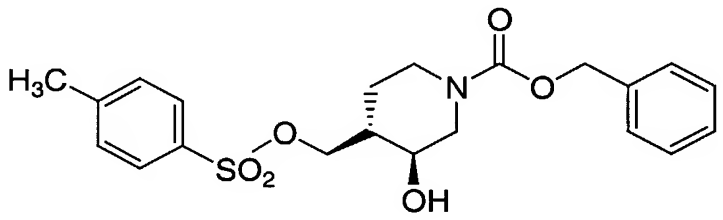


A solution of the 1-Benzyl-4-hydroxymethyl-piperidin-3-ol from **Step 1** above (13.5g) in methanol (450mL) was hydrogenated at 50psi over 20% palladium hydroxide on charcoal (10g) for 48h in three batches. The combined reaction mixtures were filtered and the filtrate evaporated to give an oil. This oil was dissolved in water (100mL) and dioxane (100mL), cooled to 5°C, and benzyl chloroformate (7.8mL) was added slowly. 1M NaOH was added to maintain pH of 10-11. After 30min, the cooling bath was removed and reaction mixture stirred for 30min. The reaction mixture was concentrated to remove dioxane and the residue extracted with EtOAc (x3). The combined extracts were washed with brine, dried over anhydrous sodium sulfate and solvent evaporated to give a mixture of cis and trans products. Purified by flash column chromatography (80% EtOAc hexane to 5% MeOH EtOAc) gave the upper Rf cis isomer and the lower Rf trans isomer.

M.S. (M+1): 266.

Step 3:

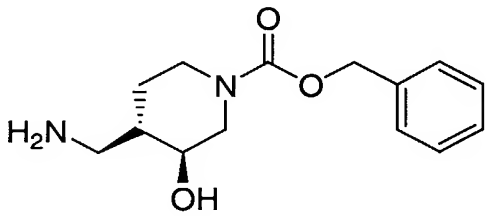
Cis 3-Hydroxy-4-(toluene-4-sulfonyloxymethyl)-piperidine-1-carboxylic acid benzyl ester



A solution of the 3-Hydroxy-4-hydroxymethyl-piperidine-1-carboxylic acid benzyl ester diol from **Step 2** above (7.65g) in chloroform (200mL) was treated with pyridine (2.6mL) and 4-toluenesulfonyl chloride (6.05g) and the reaction mixture heated to 60°C for 18h. Additional pyridine (0.85mL) and 4-toluenesulfonyl chloride (2.0g) were added to the cooled reaction and heating continued for a further 24h. The reaction mixture was cooled to rt and washed with 10% aqueous citric acid solution and water, dried over anhydrous sodium sulfate and the solvent evaporated to give, after flash column chromatography, the Cis 3-Hydroxy-4-(toluene-4-sulfonyloxymethyl)-piperidine-1-carboxylic acid benzyl ester.

Step 4:

Cis 4-Aminomethyl-3-hydroxy-piperidine-1-carboxylic acid benzyl ester

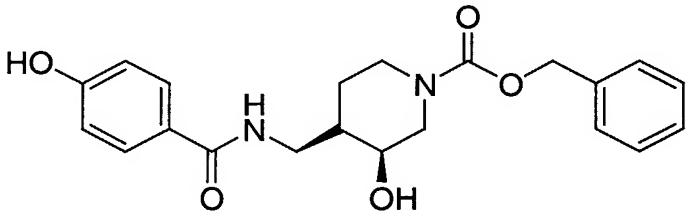


A solution of the cis 3-Hydroxy-4-(toluene-4-sulfonyloxymethyl)-piperidine-1-carboxylic acid benzyl ester (6.80g) from **Step 3** above was dissolved in DMF (50mL) and treated with sodium azide (3.16g). The reaction mixture was then heated to 50°C for 48h, cooled to rt, and partitioned between dilute aqueous sodium bicarbonate and EtOAc. The organic layer was washed with brine, dried over anhydrous sodium sulfate and solvent evaporated to give the azide, which was dissolved in THF (50mL) and treated with triphenylphosphine (14.07g) and water (3.25mL). The reaction mixture was stirred for 18h at rt, the volatiles evaporated, and the residue purified by flash column chromatography (DCM to 80/20/2 DCM MeOH NH_4OH) to give the cis 4-Aminomethyl-3-hydroxy-piperidine-1-carboxylic acid benzyl ester as an oil.

M.S. (M+1): 265.

Step 4:

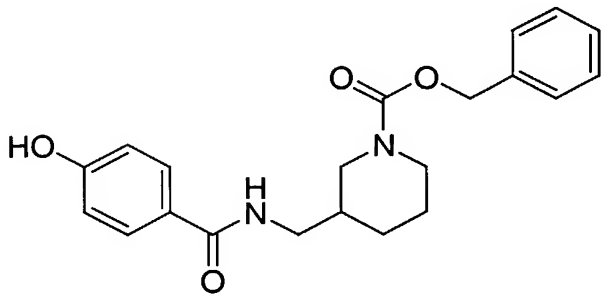
3-Hydroxy-4-[(4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester



The 3-Hydroxy-4-[(4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester was prepared from the cis 4-Aminomethyl-3-hydroxy-piperidine-1-carboxylic acid benzyl ester (**Step 3** above) and 4-hydroxybenzoic acid as described in **EXAMPLE 1, Step 2.**

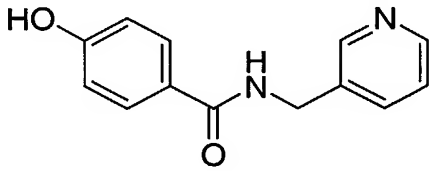
EXAMPLE 198:

3-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester



Step 1:

4-Hydroxy-N-pyridin-3-ylmethyl-benzamide

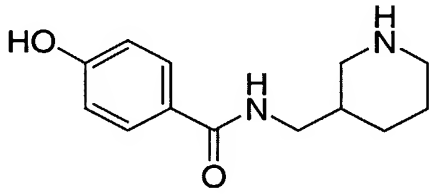


The 4-hydroxy-N-pyridin-3-ylmethyl-benzamide was prepared from 3-(2-aminomethyl)pyridine and 4-hydroxybenzoic acid in as described in **EXAMPLE 1, Step 2**.

M.S. (M+1): 229.

Step 2:

4-Hydroxy-N-piperidin-3-ylmethyl-benzamide



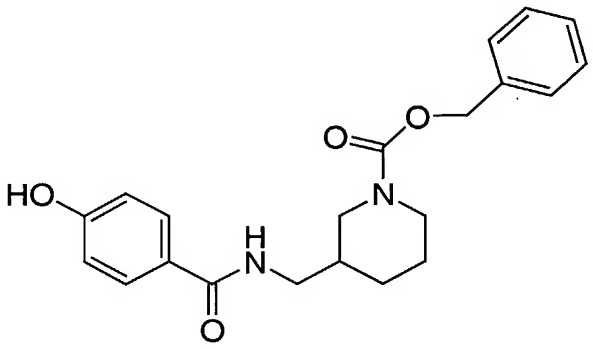
To a solution of 4-hydroxy-N-pyridin-3-ylmethyl-benzamide (2.0g, 0.0088mol) in acetic acid (135mL) was added platinum oxide (200mg) and the

mixture stirred under hydrogen for 3h. The reaction was filtered and concentrated *in vacuo* to give an oil.

M.S. (M+1): 235.

Step 3:

3-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester

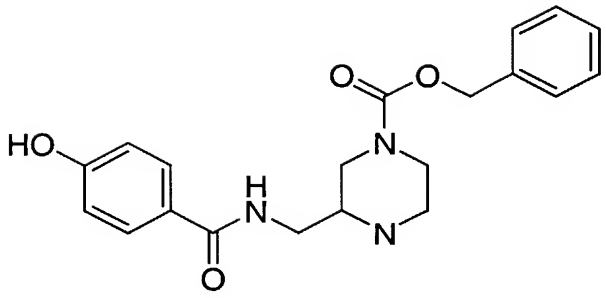


To a mixture of 4-hydroxy-N-piperidin-3-ylmethyl-benzamide (135mg, 0.580mmol) in tetrahydrofuran (5mL) was added triethylamine (100μL) and N-benzyloxycarbonyloxysuccinamide (144mg, 0.580mmol) and the mixture stirred at rt for 3h. The reaction was concentrated *in vacuo* and chromatographed on silica using 50-100% ethyl acetate/hexane to give 3-[(4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester as a foam.

M.S. (M+1): 369.

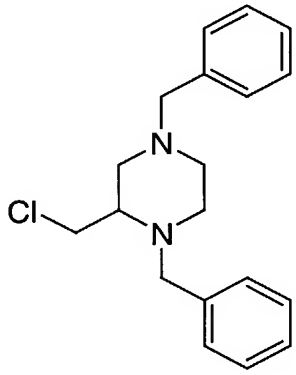
EXAMPLE 199:

3-[(4-Hydroxy-benzoylamino)-methyl]-piperazine-1-carboxylic acid benzyl ester



Step 1:

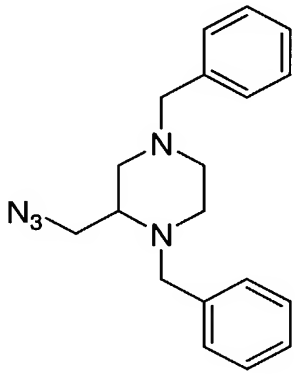
1,4-Dibenzyl-2-chloromethyl-piperazine



The above compound was prepared according to the procedure described in Bihan, G. et. al., *J. Med. Chem.*, 42:1587-1603(1999).

Step 2:

2-Azidomethyl-1,4-dibenzyl-piperazine

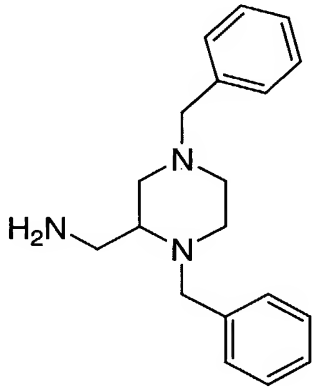


To a solution of 1,4-dibenzyl-2-chloromethyl-piperazine (8.8g, 0.028mol) in dimethylformamide (90mL) under nitrogen was added sodium azide (5.5g) and the reaction stirred at 50°C for 18h. The reaction was cooled and diluted with 10% aqueous sodium bicarbonate (100mL) and water (250mL) and the mixture extracted with ethyl acetate (2 X 200mL). The organic extracts were washed with 10% sodium bicarbonate, brine, dried over sodium sulfate and concentrated to an oil.

M.S. (M+1): 322.

Step 3:

C-(1,4-Dibenzyl-piperazin-2-yl)-methylamine

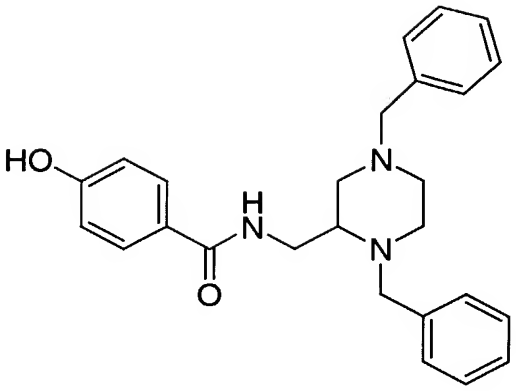


To a solution of 2-azidomethyl-1,4-dibenzyl-piperazine (9.0g, 0.028mol) in THF (90mL) and water (5mL) was added triphenylphosphine (22.3g, 0.085mol) and the mixture stirred for 18h. The reaction was concentrated to an oil, dissolved in 1N hydrochloric acid (100mL) and washed with ethyl acetate (2x100mL). The acidic aqueous layer was cooled to 0°C and the pH adjusted to 8.5 with 3N sodium hydroxide. The mixture was extracted with ethyl acetate (2x100mL) and extracts dried over sodium sulfate and concentrated to an oil.

M.S. (M+1): 296.

Step 4:

N-(1,4-Dibenzyl-piperazin-2-ylmethyl)-4-hydroxy-benzamide

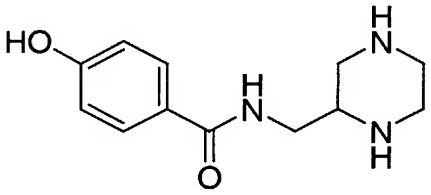


The N-(1,4-Dibenzyl-piperazin-2-ylmethyl)-4-hydroxy-benzamide was prepared from C-(1,4-Dibenzyl-piperazin-2-yl)-methylamine and 4-hydroxybenzoic acid as described in **EXAMPLE 1, Step 2**.

M.S. (M+1): 416.

Step 5:

4-Hydroxy-N-piperazin-2-ylmethyl-benzamide

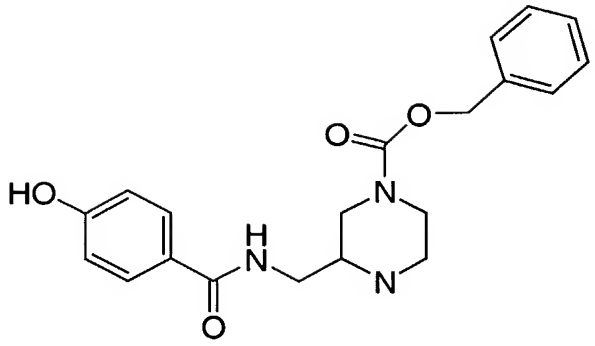


The 4-Hydroxy-N-piperazin-2-ylmethyl-benzamide was prepared according to the procedure described in **EXAMPLE 198, Step 2**, using 10% Palladium/Carbon as catalyst in ethanol/12N HCl at 50°C for 5h.

M.S. (M+1): 236.

Step 6:

3-[(4-Hydroxy-benzoylamino)-methyl]-piperazine-1-carboxylic acid benzyl ester

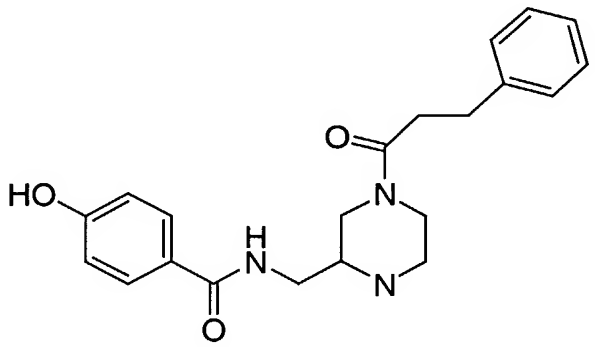


The 3-[(4-Hydroxy-benzoylamino)-methyl]-piperazine-1-carboxylic acid benzyl ester was prepared according to the procedure described in **EXAMPLE 198, Step 3**. Dilution of reaction with 10% aqueous sodium bicarbonate and extraction with ethyl acetate followed by concentration and purification by silica gel chromatography using 95/5/1 to 90/10/2 (dichloromethane/methanol/NH_4OH) gave the 3-[(4-Hydroxy-benzoylamino)-methyl]-piperazine-1-carboxylic acid benzyl ester as a solid.

M.S. (M+1): 370.

EXAMPLE 200:

4-Hydroxy-N-[4-(3-phenyl-propionyl)-piperazin-2-ylmethyl]-benzamide

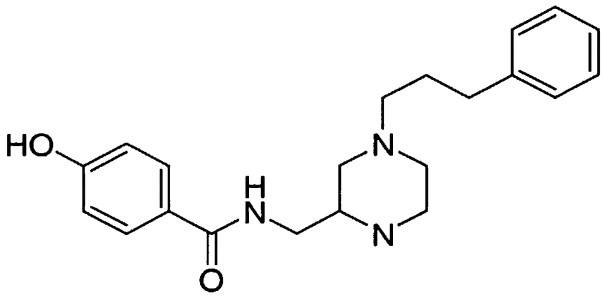


The title compound was prepared in a similar manner as described in **EXAMPLE 1, Step 2**, from 4-hydroxy-N-piperazin-2-ylmethyl-benzamide and 4-hydroxybenzoic acid.

M.S. (M+1): 368.

EXAMPLE 201:

4-Hydroxy-N-[4-(3-phenyl-propyl)-piperazin-2-ylmethyl]-benzamide

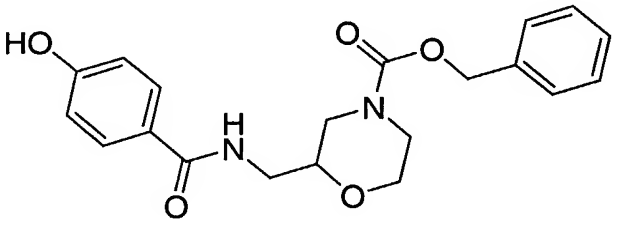


The title compound was prepared in a similar manner as described in **EXAMPLE 148, Step 1**, from 4-Hydroxy-N-piperazin-2-ylmethyl-benzamide and propionaldehyde in dichlorethane as solvent.

M.S. (M+1): 354.

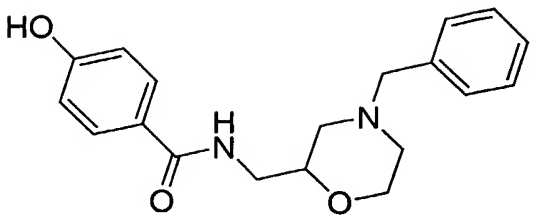
EXAMPLE 202:

2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid benzyl ester



Step 1:

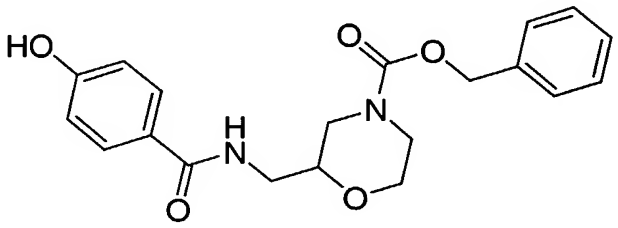
N-(4-Benzyl-morpholin-2-ylmethyl)-4-hydroxy-benzamide



The N-(4-Benzyl-morpholin-2-ylmethyl)-4-hydroxy-benzamide was prepared from C-(4-benzyl-morpholin-2-yl)-methylamine (S. Kato et al., *J. Med Chem.*, 33:1406(1990)) similarly to the procedure described in **EXAMPLE 1, Step 2.**

M.S. (M+1): 327

Step 2:

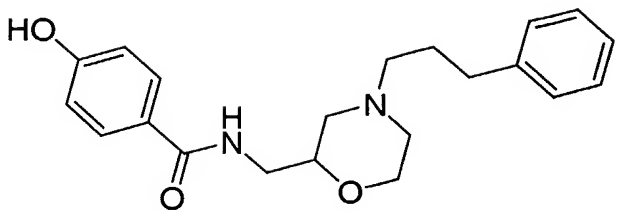


A solution of N-(4-benzyl-morpholin-2-ylmethyl)-4-hydroxy-benzamide (**Step 1** above) (320mg) was dissolved in ethanol (20mL) and hydrogenated at 1atm over 20% $Pd(OH)_2/C$ (250mg) for 18h. The catalyst was removed by filtration, washed with ethanol, and the filtrate evaporated, to give a solid. A portion (21mg) of this material was dissolved in DMF (0.5mL) and N-(benzyloxycarbonyloxy)succinimide (27mg) was added. The reaction mixture was stirred for 10min, one drop of water was added and the solution was purified by preparative reverse phase HPLC to give the 2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid benzyl ester compound.

M.S. (M+1): 371

EXAMPLE 203:

4-Hydroxy-N-[4-(3-phenyl-propyl)-morpholin-2-ylmethyl]-benzamide

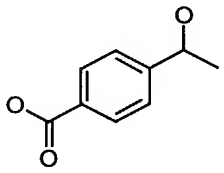


A solution of N-(4-benzyl-morpholin-2-ylmethyl)-4-hydroxy-benzamide (**EXAMPLE 202, Step 1**) (55mg) was dissolved in acetic acid (3mL) and hydrogenated at 1atm over 10% Pd/C (50mg) for 18h. The catalyst was removed by filtration, washed with acetic acid and the filtrate evaporated, to give an oil. A portion of this oil (21mg) was dissolved in methanol (1mL) and treated with phenylpropionaldehyde (24mg) and sodium cyanoborohydride (25mg). The resulting reaction was stirred for 15min and the crude reaction mixture purified by preparative reverse phase HPLC to give the 4-Hydroxy-N-[4-(3-phenyl-propyl)-morpholin-2-ylmethyl]-benzamide compound.

M.S. (M+1): 355

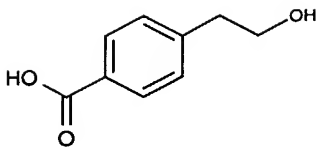
ACID INTERMEDIATES:

4-(1-Hydroxyethyl)benzoic acid:



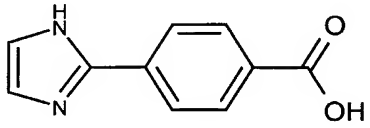
To a solution of methyl 4-(1-hydroxyethyl)benzoate (150mg, 0.83mmol) in THF (1mL) was added 1M LiOH (1mL). The reaction mixture was heated to 60°C and stirred for 1h. After cooling, the reaction was acidified with 1M HCl, and extracted with EtOAc twice. The organic layer was dried over Na_2SO_4, filtered and concentrated to give 4-(1-hydroxyethyl)benzoic acid as a white solid which was used without further purification.

4-(2-Hydroxyethyl)benzoic acid:



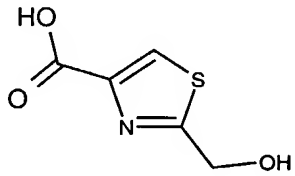
To a solution of 0.5g (3.40mmol) of the nitrile and 20mL ethanol was added 7mL of 2N NaOH. The solution was heated at 98°C for 18h., cooled, then evaporated. The remaining oil was dissolved into EtOAc and aqueous sodium bicarbonate. The organic layer was discarded. The aqueous layer was acidified with 6N HCl, extracted into EtOAc, dried over Na_2SO_4, filtered and evaporated to yield the hydroxy acid as a white solid.

4-(1H-Imidazol-2-yl)benzoic acid:



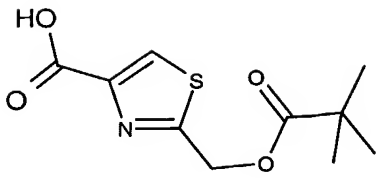
Ammonia gas was bubbled into a solution of 4-carboxybenzaldehyde (2.0g, 13.32mmol) in water (15mL) for 10min.. To clear soln was added glyoxal (2.9mL, 19.98mmol) in water (10mL) dropwise over 15min and the reaction mixture was stirred for 3h. The solution was neutralized with 6N HCl and filtered to give a white paste. Trituration with acetone followed by evaporation gave 4-(1H-imidazol-2-yl)benzoic acid as a white solid.

2-(Hydroxymethyl)-1,3-thiazole-4-carboxylic acid:



Step 1:

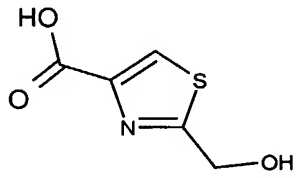
Preparation of 2-{[(2,2-dimethylpropanoyl)oxy]methyl}-1,3-thiazole-4-carboxylic acid:



To a solution of bromopyruvic acid (0.37g, 2.22mmol) and 2-(tert-butylcarbonyloxy)thioacetamide (0.41g, 2.22mmol) in ethanol (20mL) was added 4 A molecular sieves (2 g). After stirring for 15h, 20 mL of dichloromethane was added. The mixture was stirred 5min and filtered to give the product as a yellow solid.

Step 2:

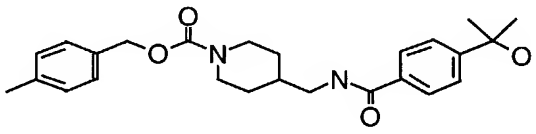
Preparation of 2-(hydroxymethyl)-1,3-thiazole-4-carboxylic acid:



To the protected alcohol acid (0.36g, 1.48mmol) in MeOH (20mL) and water (6mL) was added potassium carbonate (0.36g, 0.26mmol). The mixture was heated at reflux for 2h. The methanol was removed in vacuo and the remaining aqueous reaction mixture was extracted with hot EtOAc (2x100mL). The combined organic layers were dried over Na_2SO_4, filtered and evaporated to a yellow oil. Diethyl ether (20 mL) was added, and the mixture was decanted and dried in vacuo to give the product as a brown powder.

EXAMPLE 204:

4-Methylbenzyl 4-({[4-(1-hydroxy-1-methylethyl)benzoyl]amino}methyl)piperidine-1-carboxylate



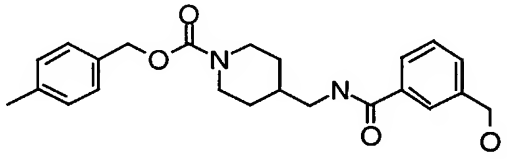
To a 0°C solution of 4-methylbenzyl 4-({[4-(methoxycarbonyl)benzoyl]-amino}methyl)-piperidine-1-carboxylate (**EXAMPLE 538**) (100mg, 0.24mmol) in THF (3mL) was added methyl magnesiumbromide

(0.39mL, 1.18mmol, 3.0M in Et_2O). The reaction mixture was warmed to rt, quenched with H_2O and extracted with EtOAc. The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was chromatographed on silica gel (gradient elution, 2:1 hexane:EtOAc to EtOAc) to give 4-methylbenzyl 4-({[4-(1-hydroxy-1-methylethyl)benzoyl]amino}methyl)piperidine-1-carboxylate.

$(M+H)^+ = 425.5$

EXAMPLE 205:

4-Methylbenzyl 4-({[3-(hydroxymethyl)benzoyl]amino}methyl)piperidine-1-carboxylate

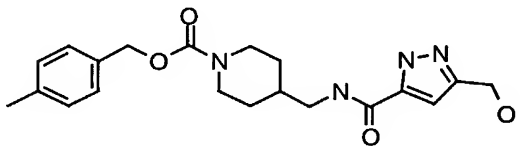


To a solution of 4-methylbenzyl 4-({[3-(methoxycarbonyl)benzoyl]amino}methyl)piperidine-1-carboxylate (**EXAMPLE 540**) (100mg, 0.24mmol) in MeOH (2mL) was added sodium borohydride (0.18mg, 4.7mmol). The solution was stirred at rt for 2h, quenched with saturated NH_4Cl (aq) and extracted with EtOAc. The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was chromatographed on silica gel (gradient elution, 2:1 hexane:EtOAc to EtOAc) to give 4-methylbenzyl 4-({[3-(hydroxymethyl)benzoyl]amino}methyl)piperidine-1-carboxylate.

$(M+H)^+ = 397.5$

EXAMPLE 206:

4-Methylbenzyl 4-[({[3-(hydroxymethyl)-1H-pyrazol-5-yl]carbonyl}amino)methyl]piperidine-1-carboxylate



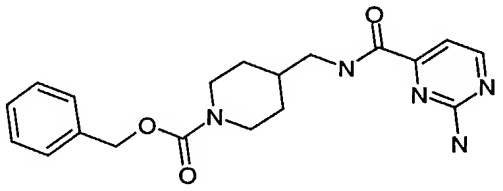
To 5-({[(1-{[(4-methylbenzyl)oxy]carbonyl}piperidin-4-yl)methyl]amino}carbonyl)-1H-pyrazole-3-carboxylic acid (50mg, 0.13mmol) was

added BH_3-THF solution (2.5mL, 2.5mmol, 1.0M in THF). The solution was stirred at rt for 1h, quenched with HCl (1M) and extracted with EtOAc. The organic layer was washed with H_2O dried over Na_2SO_4, filtered and concentrated. The residue was chromatographed on silica gel (gradient elution, EtOAc to 10% MeOH/EtOAc) to give 4-methylbenzyl 4-[({[3-(hydroxymethyl)-1H-pyrazol-5-yl]carbonyl}amino)methyl]piperidine-1-carboxylate.

$(M+H)^+ = 387.5$

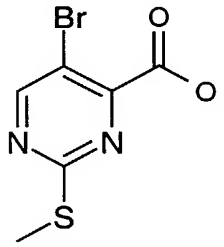
EXAMPLE 207:

Benzyl 4-({[(2-aminopyrimidin-4-yl)carbonyl]amino}-methyl)piperidine-1-carboxylate



Step 1:

Preparation of 5-bromo-2-(methylthio)pyrimidine-4-carboxylic acid:

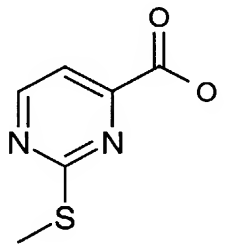


To a stirring solution of mucobromic acid (28.1g, 109mmol) and 2-methyl-2-thiopseudourea sulfate (21.4g, 109mmol) in water (400mL) under an argon atmosphere was added triethylamine (45.6mL, 327mmol) via a syringe pump (~3mL/h). After 18h, conc. HCl (14mL) was added to the dark brown solution, stirred 30min, then filtered. The resulting solid was washed with water and dried to yield a brown solid. The solid was dissolved in 400mL water, and the pH was adjusted to ~8 with solid sodium bicarbonate slowly to form a solution. To the solution, 10g of

Norit decolorizing charcoal was added and the suspension was heated for1.25h. at 100°C, cooled, then filtered through a pad of Celite. The pH of the solution was adjusted to ~0.3 with conc. HCl, allowed to stir in an ice bath for 30min then filtered to yield 16.0g of yellow solid after drying in air.

Step 2:

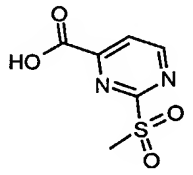
Preparation of 2-(methylthio)pyrimidine-4-carboxylic acid



A solution of 5-bromo-2-(methylthio)pyrimidine-4-carboxylic acid (8.0g, 32.1mmol) and potassium hydroxide (4.4g, 32.1mmol) in MeOH (175mL) was transferred to a Parr hydrogenation jar. After purging the solution with nitrogen gas, of 5% Pd on barium sulfate (3.93g) was added then hydrogenated on Parr Hydrogenation Apparatus for 2h at 40 psi. The mixture was filtered through a Celite pad. The resulting yellow solution was evaporated to ~30mL, then conc HCl was added to pH~ 0.3, yielding a yellow solid carboxylic acid after filtration and air drying.

Step 3:

Preparation of 2-(methylsulfonyl)pyrimidine-4-carboxylic acid:

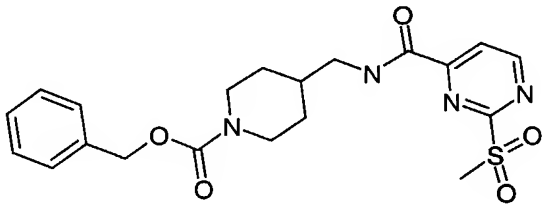


To a solution of 2-(methylthio)pyrimidine-4-carboxylic acid (1.88g (11.1mmol) in THF (200mL) was added Oxone (20.4g , 33.1mmol) in water (50mL). The suspension was stirred for 24h, then evaporated to dryness. The resulting white paste was extracted 5x each 100mL EtOAc and 5% MeOH in EtOAc. The combined

extracts were dried over anhydrous $MgSO_4$, filtered and concentrated to give the sulfone as a white solid.

Step 4:

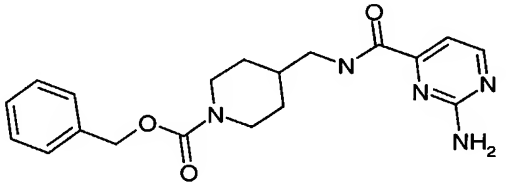
Preparation of benzyl 4-[({[2-(methylsulfonyl)pyrimidin-4-yl]carbonyl}amino)methyl]piperidine-1-carboxylate



2-(Methylsulfonyl)pyrimidine-4-carboxylic acid was coupled to benzyl 4-(aminomethyl)piperidine-1-carboxylate according to the procedure for **EXAMPLE 1.**

Step 5:

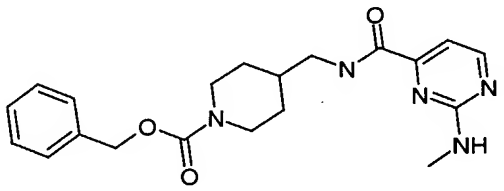
Preparation of benzyl 4-({[(2-aminopyrimidin-4-yl)carbonyl]amino}-methyl)piperidine-1-carboxylate



Ammonia gas was bubbled through a solution of benzyl 4-[({[2-(methylsulfonyl)pyrimidin-4-yl]carbonyl}amino)methyl]piperidine-1-carboxylate (**EXAMPLE 207, Step 4**) (1.30g, 3.01mmol) in EtOAc (75mL) for 10min. The resulting solution was heated in a sealed pressure tube for 18h. at 65°C. The white suspension was then concentrated in vacuo. The mixture was recrystallized using ~20mL EtOAc, and a minimal amount of MeOH, providing **EXAMPLE 207** as a white solid. $(M+H)^+ = 370.4$

EXAMPLE 208:

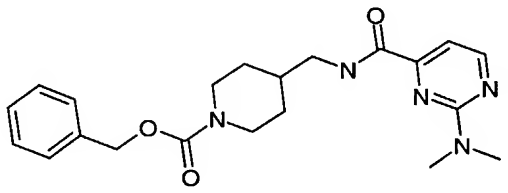
Benzyl 4-[({[2-(methylamino)pyrimidin-4-yl]carbonyl}amino)methyl]piperidine-1-carboxylate



To a solution of benzyl 4-[({[2-(methylsulfonyl)pyrimidin-4-yl]carbonyl}amino)methyl]piperidine-1-carboxylate (**EXAMPLE 207, Step 4**) (0.90g, 3.01mmol) in THF (75mL) was added 40% aqueous methylamine (0.45g). The resulting solution was heated for 18h at 65°C, evaporated to dryness and purified by silica gel chromatography (gradient elution, 30 to 100% ethyl acetate in hexane) to provide **EXAMPLE 208** as a yellow gum. $(M+H)^+ = 384.3$

EXAMPLE 209:

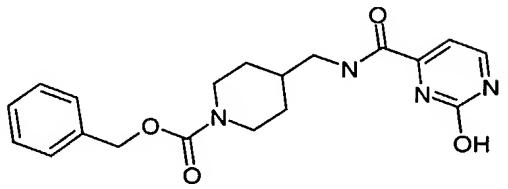
Benzyl 4-[({[2-(dimethylamino)pyrimidin-4-yl]carbonyl}amino)methyl]piperidine-1-carboxylate



To a solution of benzyl 4-[({[2-(methylsulfonyl)pyrimidin-4-yl]carbonyl}amino)methyl]piperidine-1-carboxylate (**EXAMPLE 207, Step 4**) (43mg, 0.01mmol) in THF (10mL) was added dimethylamine hydrochloride (23.6mg, 0.3mmol). The resulting solution was heated for 18h at 80°C and evaporated to dryness. Ethyl acetate was added, and washed with sat'd aqueous sodium bicarbonate, water then brine. The organic layer was dried over Na_2SO_4, filtered and concentrated. The resulting oil was purified by silica gel chromatography (gradient elution, 20 to 100% ethyl acetate in hexane) to provide **EXAMPLE 209** as a white foam. $(M+H)^+ = 398.3$

EXAMPLE 210:

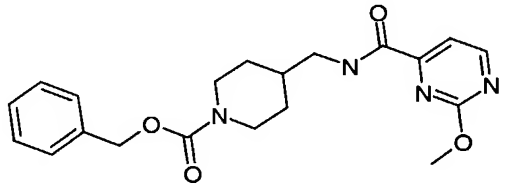
Benzyl 4-({[(2-hydroxypyrimidin-4-yl)carbonyl]amino}methyl)piperidine-1-carboxylate



To a solution of benzyl 4-[({[2-(methylsulfonyl)pyrimidin-4-yl]carbonyl}amino)methyl]piperidine-1-carboxylate (**EXAMPLE 207, Step 4**) (70mg, 0.20mmol) in THF (3mL) was added NH_4OH (0.5mL). The solution was stirred at rt for 2h. The solution was evaporated, water was added then extracted 2x with EtOAc, dried over Na_2SO_4, and evaporated to an oil. Silica gel column chromatography using a 95:5:0.5 to 90:10:1 CH_2Cl_2:MeOH:NH_4OH gradient provided **EXAMPLE 210** as a white solid. $(M+H)^+ = 371.4$

EXAMPLE 211:

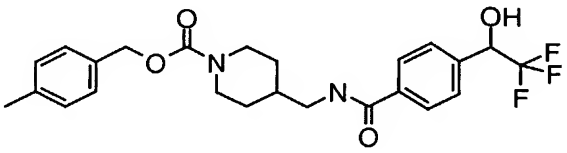
Benzyl 4-({[(2-methoxypyrimidin-4-yl)carbonyl]amino}methyl)piperidine-1-carboxylate



A solution of benzyl 4-[({[2-(methylsulfonyl)pyrimidin-4-yl]carbonyl}amino)methyl]piperidine-1-carboxylate (**EXAMPLE 207, Step 4**) (70mg, 0.20mmol) in MeOH (3mL) was heated at 60°C for 18h. The solution was evaporated, water was added then extracted 2x with EtOAc, dried over Na_2SO_4, and evaporated to an oil. Silica gel column chromatography using a 95:5:0.5 to 90:10:1 CH_2Cl_2:MeOH:NH_4OH gradient provided **EXAMPLE 211** as a white solid. $(M+H)^+ = 385.4$

EXAMPLE 212:

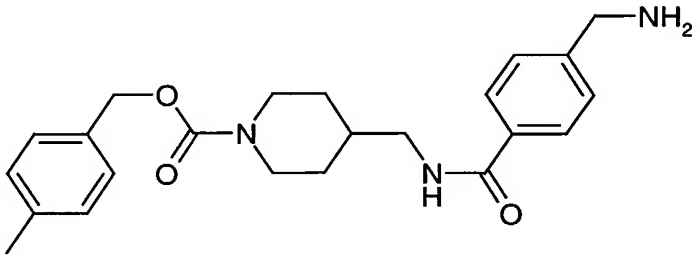
4-Methylbenzyl 4-({[4-(2,2,2-trifluoro-1-hydroxyethyl)benzoyl]amino}methyl)piperidine-1-carboxylate:



To a solution of 4-methylbenzyl 4-({[4-(trifluoroacetyl)benzoyl]amino}methyl)piperidine-1-carboxylate (**EXAMPLE 543**) (250mg, 0.54mmol) in methanol (10mL) was added sodium borohydride (20.5mg, 0.54mmol). After 1h., water (10mL) was added and the organics evaporated. The aqueous suspension was extracted 2x with EtOAc. The organics were dried over Na_2SO_4, filtered and evaporated to a clear oil. Silica gel chromatography (gradient elution, 30 to 100% ethyl acetate in hexane), provided **EXAMPLE 212** as a white foam. $(M+H)^+ = 465.4$

EXAMPLE 213:

4-Methylbenzyl 4-({[4-(aminomethyl)benzoyl]amino}methyl)piperidine-1-carboxylate:

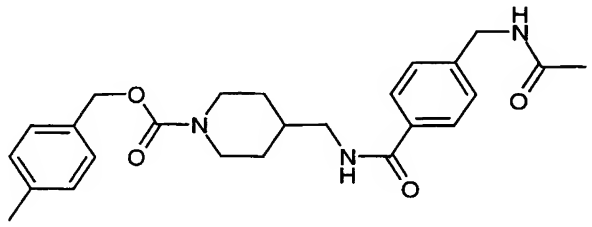


4-Methylbenzyl 4-{[(4-{[(tert-butoxycarbonyl)amino]methyl}benzoyl)amino] methyl}piperidine-1-carboxylate (**EXAMPLE 544**) (200mg, 0.40mmol) was dissolved in EtOAc (10mL), cooled to 0°C, and gaseous HCl was bubbled in for 10min. After 30min., the mixture was evaporated to give a fine white powder of the hydrochloride salt of **EXAMPLE 213**.

$(M+H)^+ = 396.4$

EXAMPLE 214:

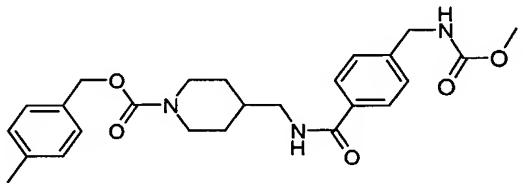
4-Methylbenzyl 4-[({4-[(acetylamino)methyl]benzoyl}amino)methyl]piperidine-1-carboxylate:



To a solution of **EXAMPLE 213** (20mg, 0.05mmol), in CH_2Cl_2 (10mL) was added triethylamine (14μL, 0.10mmol) and acetyl chloride (7.2μL, 0.092mmol). After 5min, water was added and the product was extracted into CH_2Cl_2. Evaporation gave **EXAMPLE 214** as a white solid. $(M+H)^+ = 438.3$

EXAMPLE 215:

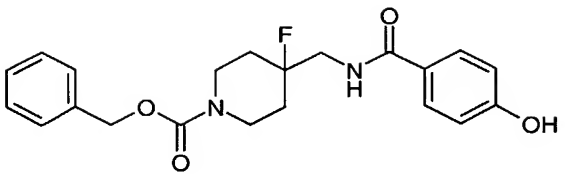
4-methylbenzyl 4-{[(4-{[(methoxycarbonyl)amino]methyl} benzoyl)amino]methyl}piperidine-1-carboxylate:



To a solution of **EXAMPLE 213** (30mg, 0.069mmol) in THF (5mL) was added triethylamine (19.3μL) and methylchloroformate (5.3μL). The reaction mixture was stirred for 3h then concentrated. Water and saturated sodium bicarbonate was added and the aqueous layer was extracted with EtOAc. The organic layer was dried over Na_2SO_4, filtered and concentrated to a white solid. Silica gel chromatography (75% ethyl acetate in hexane to 95:5:0.5 ethyl acetate:MeOH:NH_4OH) provided **EXAMPLE 215** as a white solid. $(M+H)^+ = 454.4$

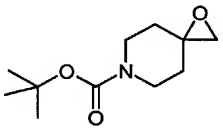
EXAMPLE 216:

Benzyl 4-fluoro-4-{[(4-hydroxybenzoyl)amino]methyl}piperidine-1-carboxylate:



Step 1:

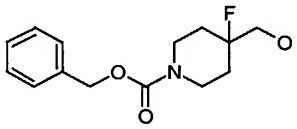
Preparation of tert-butyl 1-oxa-6-azaspiro[2.5]octane-6-carboxylate



To a solution of tert-butyl 4-oxopiperidine-1-carboxylate (0.50g, 2.51mmol) in THF/DMF (2:1, 6mL) at 60 °C was added trimethylsulfoxonium iodide (0.58g, 2.63mmol) and sodium t-butoxide (0.25g, 2.63mmol). The reaction mixture was stirred at 60 °C for 30min, cooled to rt and concentrated. Water was added and the mixture was extract with EtOAc twice. The combined organics were dried over Na_2SO_4, filtered and concentrated. Purification on silica gel (3:1, hexanes:EtOAc) gave tert-butyl 1-oxa-6-azaspiro[2.5]octane-6-carboxylate as a clear oil that solidified upon standing.

Step 2:

Preparation of benzyl 4-fluoro-4-(hydroxymethyl)piperidine-1-carboxylate

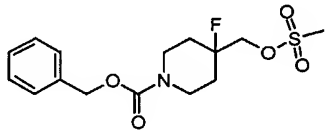


To a solution of tert-butyl 4-oxopiperidine-1-carboxylate (7.0 g, 32.8mmol) in CH_2Cl_2 (14mL) at –10 °C was added HF-pyridine (11.6mL, 82.1mmol) portionwise. The reaction mixture was stirred for 10min at –10 °C, warmed to rt. After stirring for 16h, the reaction was carefully quenched with aqueous $NaCO_3$, and extracted with CH_2Cl_2. The aquoues layer was concentrated to a white paste that was suspended in CH_2Cl_2 (100mL). BOCOS (8.2g, 32.8mmol) was added and the mixure

was stirred at RT for 3h. The reaction mixture was partitioned between EtOAc and H_2O, the organic layer was dried over Na_2SO_4, filitered and concentrated. Purification on silica gel (10:1 to 1:1 hexanes:EtOAc) gave benzyl 4-fluoro-4-(hydroxymethyl)piperidine-1-carboxylate as a clear oil.

Step 3:

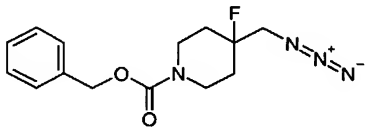
Preparation of benzyl 4-fluoro-4-{[(methylsulfonyl)oxy]methyl}piperidine-1-carboxylate



To a solution of benzyl 4-fluoro-4-(hydroxymethyl)piperidine-1-carboxylate (1.0g, 3.7mmol) in CH_2Cl_2 (10mL) at RT was added MsCl (0.29mL, 3.7mmol) and TEA (1.04mL, 7.5mmol). The reaction mixture was stirred at RT for 5min, and partitioned between EtOAc and H_2O. The organic layer was dried over Na2SO4, filtered, concentrated and purified on silica gel (10:1 to 1:2 hexanes:EtOAc) to give benzyl 4-fluoro-4-{[(methylsulfonyl)oxy]methyl}piperidine-1-carboxylate.

Step 4:

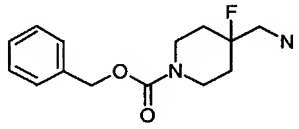
Preparation of benzyl 4-(azidomethyl)-4-fluoropiperidine-1-carboxylate



To a solution of benzyl 4-fluoro-4-{[(methylsulfonyl)oxy]methyl}piperidine-1-carboxylate (1.3g, 3.7mmol) in DMF (10mL) at RT was added NaN_3 (2.4g, 37.0mmol). The reaction mixture was heated to 110 °C and stirred for 60h, cooled and partitioned between EtOAc and H_2O. The organic layer was dried over Na_2SO_4, filtered, concentrated and purified on silica gel (10:1 to 1:2 hexanes:EtOAc) to give benzyl 4-(azidomethyl)-4-fluoropiperidine-1-carboxylate.

Step 5:

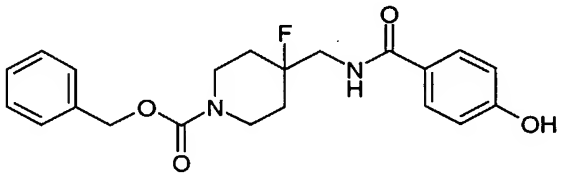
Preparation of benzyl 4-(aminomethyl)-4-fluoropiperidine-1-carboxylate



To a solution of benzyl 4-(azidomethyl)-4-fluoropiperidine-1-carboxylate (1.5g, 5.1mmol) in THF (10mL) at RT with added water (0.92mL, 0.92mmol) and triphenylphosphine (4.3g, 15.4mmol). The reaction mixture was stirred for 60h, concentrated, dissolved in HCl (1M) and extracted with Et_2O four times. The aqueous layer was basified to pH 11 and extracted with EtOAc twice. The organic layer was dried over Na_2SO_4, filtered and concentrated. The crude mixture was chromatographed on silica gel (CH_2Cl_2 to 80:20:2 CH2Cl2:MeOH:NH4OH) to give benzyl 4-(aminomethyl)-4-fluoropiperidine-1-carboxylate.

Step 6:

Benzyl 4-fluoro-4-{[(4-hydroxybenzoyl)amino]methyl}piperidine-1-carboxylate:

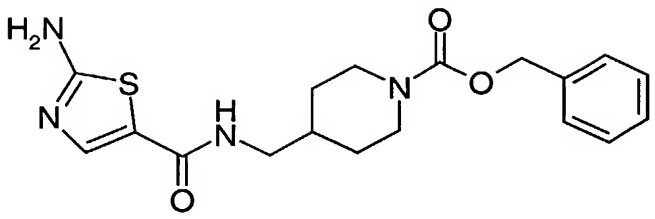


4-Hydroxy benzoic acid was coupled to benzyl 4-(aminomethyl)-4-fluoropiperidine-1-carboxylate according to the procedure for **EXAMPLE 1.**

$(M+H)^+ = 387.3$

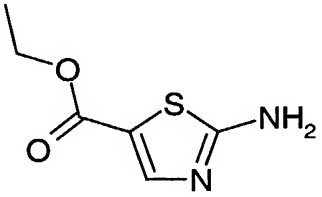
EXAMPLE 217:

Benzyl 4-({[(2-amino-1,3-thiazol-5-yl)carbonyl]amino}methyl)piperidine-1-carboxylate:



Step 1:

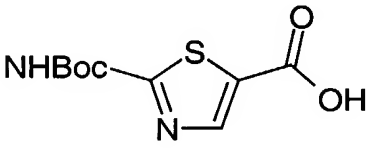
Preparation of ethyl 2-amino-1,3-thiazole-5-carboxylate:



To a mixture of β-ethoxyacrylic acid ethyl ester (2.0g, 13.9mmol) in 1:1 dioxane/water (15mL) at -10°C was added NBS (2.72g, 15.3mmol). Thiourea (1.06g, 13.9mmol) was added and the mixture was heated to 80°C and stirred for 1.5h. The reaction mixture was cooled to 0°C and 5mL of saturated ammonium hydroxide was added. A precipitate formed in 15min. The solid was filtered, washed with water and dried under vacuum, yielding a light orange solid.

Step 2:

Preparation of 2-[(tert-butoxycarbonyl)amino]-1,3-thiazole-5-carboxylic acid:

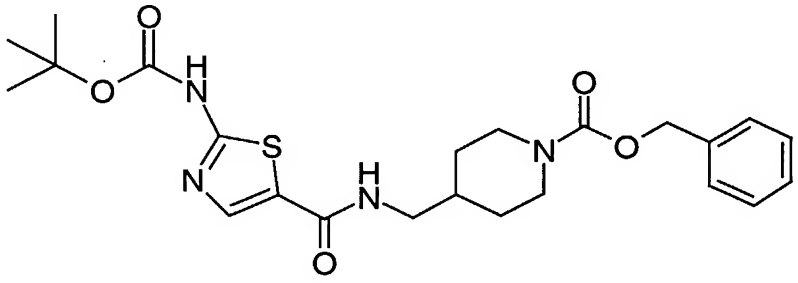


To a solution of ethyl 2-amino-1,3-thiazole-5-carboxylate (1.88g, 10.9mmol) in dioxane (100mL) was added di-*t*-butyl dicarbonate (2.43g, 12.0mmol) and 2N NaOH (16.4mL, 32.8mmol). The reaction mixture was stirred 18h. then concentrated *in vacuo*. The paste was partitioned between ethyl acetate and water, the layers were separated, and the aqueous re-extracted twice with ethyl acetate. The combined organics were dried over anhydrous sodium sulfate and concentrated to

give an oil. The product was preabsorbed onto silica gel and column chromatography (10 to 30% ethyl acetate in hexanes) afforded 3g white solid. The solid was added to a solution of lithium hydroxide (0.5g) in water/THF (1:1, 100 mL). The mixture was heated at 45°C for 3d. The organics were evaporated, and the product was partitioned between ethyl acetate and water. The aqueous layer was then acidified to pH~4 with 6N HCl and filtered to obtain an off white solid.

Step 3:

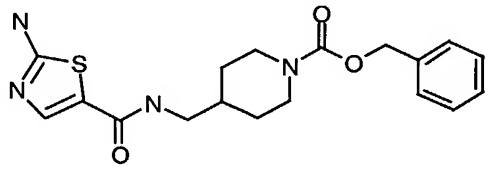
Preparation of benzyl 4-{[({2-[(tert-butoxycarbonyl)amino]-1,3-thiazol-5-yl}carbonyl)amino]methyl}piperidine-1-carboxylate:



2-[(tert-Butoxycarbonyl)amino]-1,3-thiazole-5-carboxylic acid was coupled to benzyl 4-(aminomethyl)piperidine-1-carboxylate according to the procedure for **EXAMPLE 1.**

Step 4:

Benzyl 4-({[(2-amino-1,3-thiazol-5-yl)carbonyl]amino}methyl)piperidine-1-carboxylate:

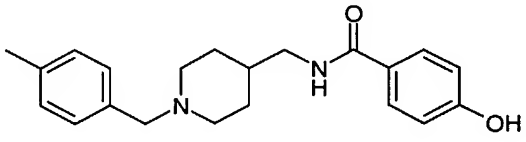


EXAMPLE 217 was prepared from benzyl 4-{[({2-[(tert-butoxycarbonyl)amino]-1,3-thiazol-5-yl}carbonyl)amino]methyl}piperidine-1-carboxylate using the procedure for **EXAMPLE 174, Step3.**

$(M+H)^+ = 375.3$

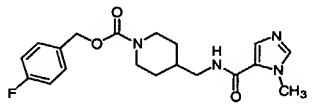
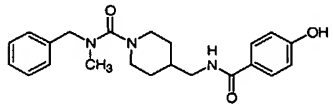
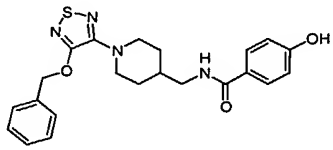
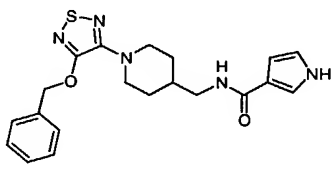
EXAMPLE 218:

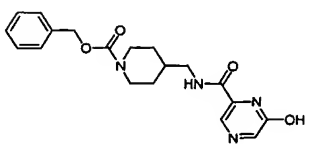
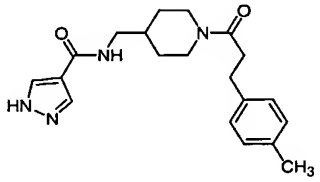
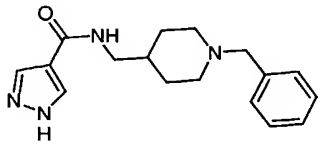
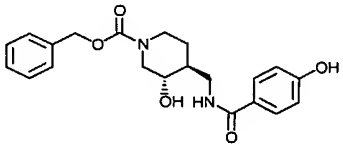
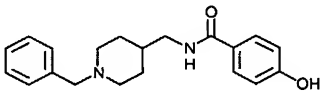
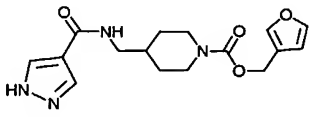
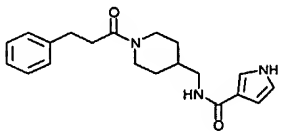
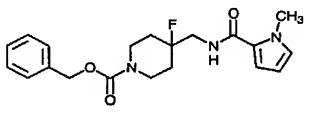
4-Hydroxy-N-{[1-(4-methylbenzyl)piperidin-4-yl]methyl}benzamide:

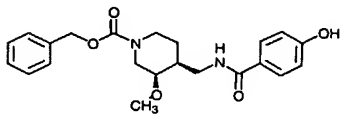
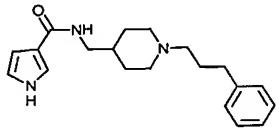
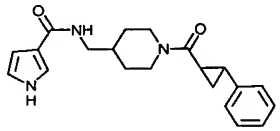
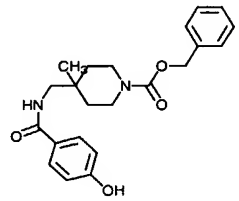
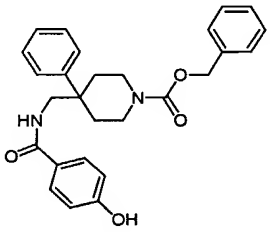
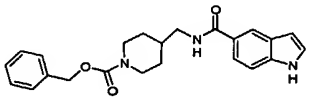
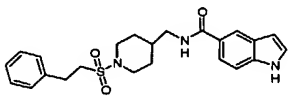


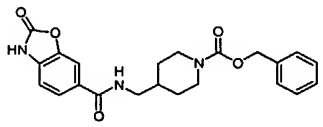
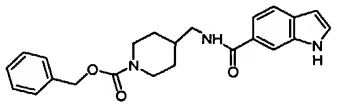
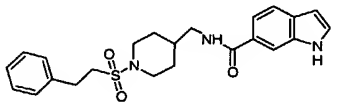
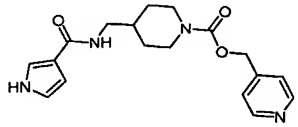
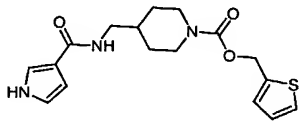
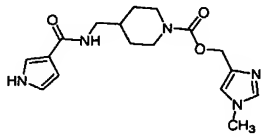
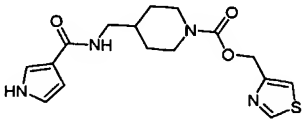
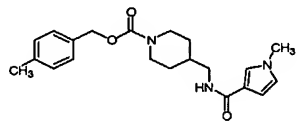
To a solution of 4-hydroxy-N-piperidin-4-ylmethyl-benzamide (**EXAMPLE 154, Step 1**) (50mg, 0.21mmol) in MeOH (3mL) was added 4-methylbenzaldehyde (25mg, 0.21mmol) and sodium cyanoborohydride (40mg, 0.64mmol). The reaction mixture was stirred at rt for 15 h, concentrated and purified by reverse-phase HPLC. $(M+H)^+ = 339.2$

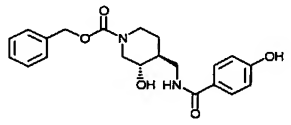
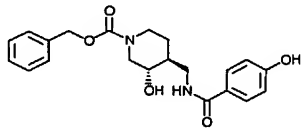
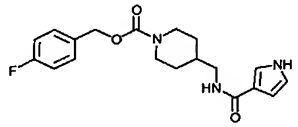
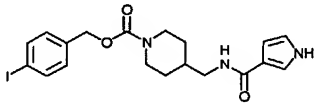
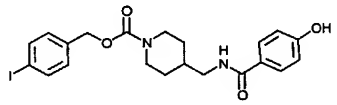
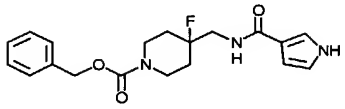
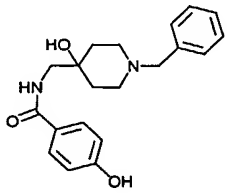
The following Examples were prepared utilizing appropriate procedures from examples described above.

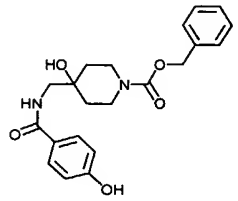
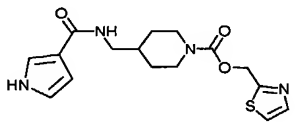
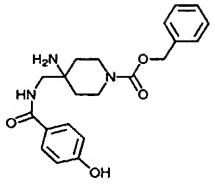
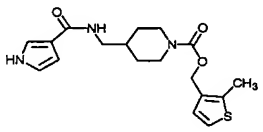
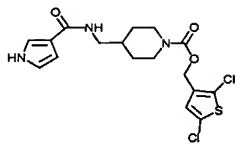
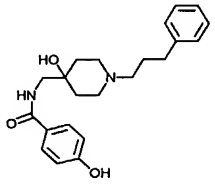
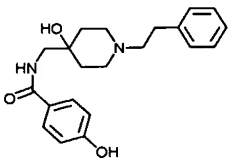
EX.	Structure	Name	MS (M^++1)
219.		4-{[(3-Methyl-3H-imidazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-fluoro-benzyl ester	375.3
220.		4-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl-methyl-amide	382.4
221.		N-[1-(4-Benzyloxy-[1,2,5]thiadiazol-3-yl)-piperidin-4-ylmethyl]-4-hydroxy-benzamide	425.2
222.		1H-Pyrrole-3-carboxylic acid [1-(4-benzyloxy-[1,2,5]thiadiazol-3-yl)-piperidin-4-ylmethyl]-amide	398.2

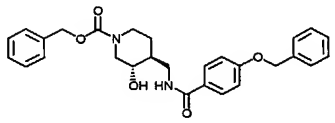
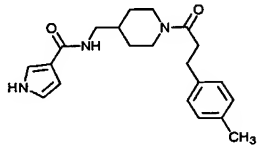
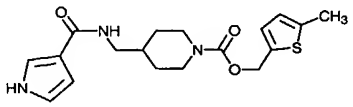
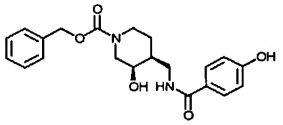
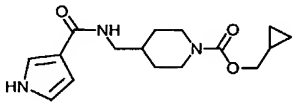
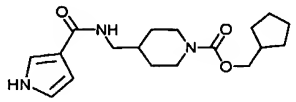
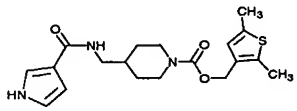
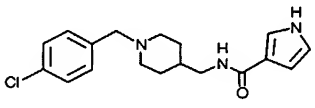
EX.	Structure	Name	MS (M^++1)
223.		4-{[(6-Hydroxy-pyrazine-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	371.3
224.		1H-Pyrazole-4-carboxylic acid [1-(3-p-tolyl-propionyl)-piperidin-4-ylmethyl]-amide	355.3
225.		1H-Pyrazole-4-carboxylic acid (1-benzyl-piperidin-4-ylmethyl)-amide	299.3
226.		3-Hydroxy-4-[(4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester	385.3
227.		N-(1-Benzyl-piperidin-4-ylmethyl)-4-hydroxy-benzamide	325.3
228.		4-{[(1H-Pyrazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid furan-3-ylmethyl ester	333.2
229.		1H-Pyrrole-3-carboxylic acid [1-(3-phenyl-propionyl)-piperidin-4-ylmethyl]-amide	340.3
230.		4-Fluoro-4-{[(1-methyl-1H-pyrrole-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	374.3

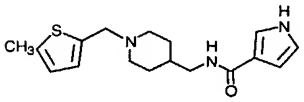
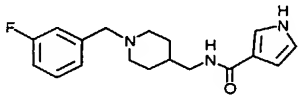
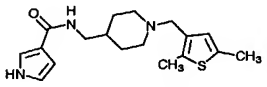
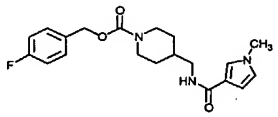
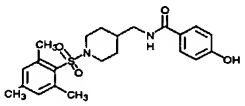
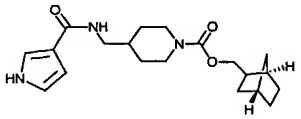
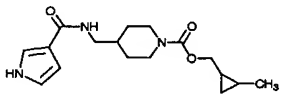
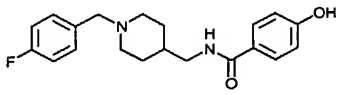
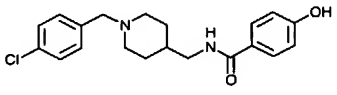
EX.	Structure	Name	MS (M^++1)
231.		4-[(4-Hydroxy-benzoylamino)-methyl]-3-methoxy-piperidine-1-carboxylic acid benzyl ester	399.3
232.		1H-Pyrrole-3-carboxylic acid [1-(3-phenyl-propyl)-piperidin-4-ylmethyl]-amide	326.3
233.		1H-Pyrrole-3-carboxylic acid [1-(2-phenyl-cyclopropanecarbonyl)-piperidin-4-ylmethyl]-amide	352.3
234.		4-[(4-Hydroxy-benzoylamino)-methyl]-4-methyl-piperidine-1-carboxylic acid benzyl ester	383.3
235.		4-[(4-Hydroxy-benzoylamino)-methyl]-4-phenyl-piperidine-1-carboxylic acid benzyl ester	445.3
236.		4-{[(1H-Indole-5-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	392.3
237.		1H-Indole-5-carboxylic acid [1-(2-phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-amide	426.3

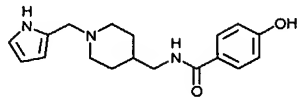
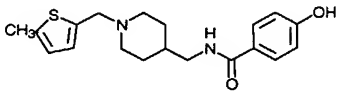
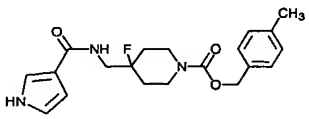
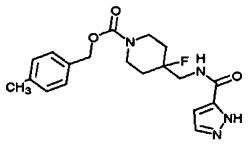
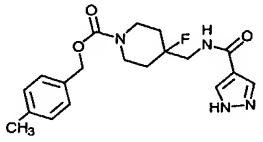
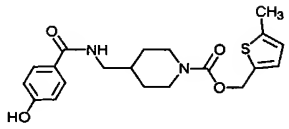
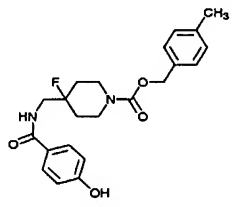
EX.	Structure	Name	MS (M^++1)
238.		4-{[(2-Oxo-2,3-dihydro-benzooxazole-6-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	
239.		4-{[(1H-Indole-6-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	392.3
240.		1H-Indole-6-carboxylic acid [1-(2-phenyl-ethanesulfonyl)-piperidin-4-ylmethyl]-amide	426.3
241.		4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid pyridin-4-ylmethyl ester	343.2
242.		4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid thiophen-2-ylmethyl ester	348.2
243.		4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 1-methyl-1H-imidazol-4-yl methyl ester	346.2
244.		4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid thiazol-4-ylmethyl ester	349.2
245.		4-{[(1-Methyl-1H-pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	370.3

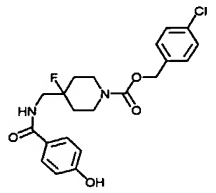
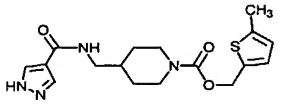
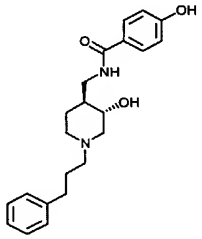
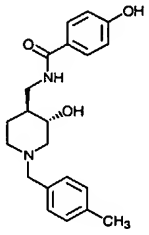
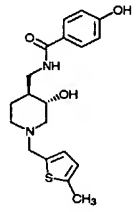
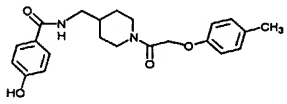
EX.	Structure	Name	MS (M^++1)
246.		3-Hydroxy-4-[(4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester	385.3
247.		3-Hydroxy-4-[(4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester	385.3
248.		4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-fluoro-benzyl ester	360.2
249.		4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-iodo-benzyl ester	468.2
250.		4-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid 4-iodo-benzyl ester	495.2
251.		4-Fluoro-4-{[(1H-pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	360.2
252.		N-(1-Benzyl-4-hydroxy-piperidin-4-ylmethyl)-4-hydroxy-benzamide	341.2

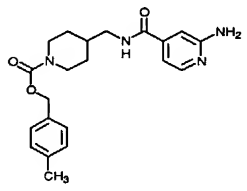
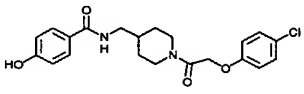
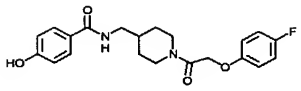
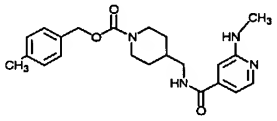
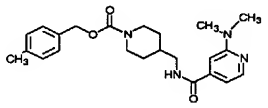
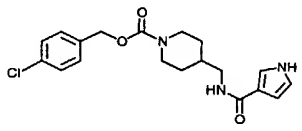
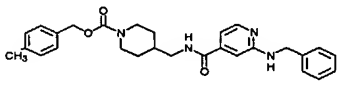
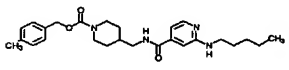
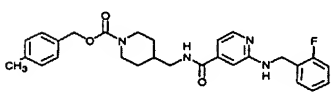
EX.	Structure	Name	MS (M^++1)
253.		4-Hydroxy-4-[(4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester	385.2
254.		4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid thiazol-2-ylmethyl ester	349.2
255.		4-Amino-4-[(4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester	384.3
256.		4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 2-methyl-thiophen-3-ylmethyl ester	362.2
257.		4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 2,5-dichloro-thiophen-3-yl methyl ester	416.1
258.		4-Hydroxy-N-[4-hydroxy-1-(3-phenyl-propyl)-piperidin-4-ylmethyl]-benzamide	369.2
259.		4-Hydroxy-N-(4-hydroxy-1-phenethyl-piperidin-4-ylmethyl)-benzamide	355.2

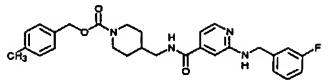
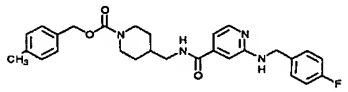
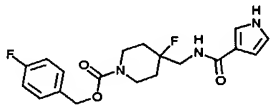
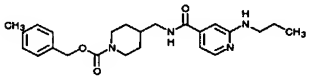
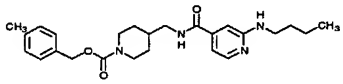
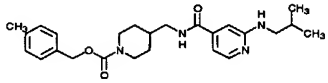
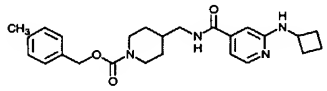
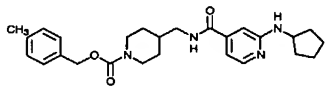
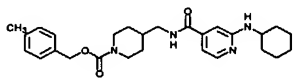
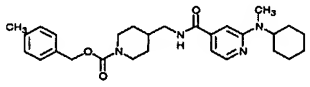
EX.	Structure	Name	MS (M^++1)
260.		4-[(4-Benzyloxy-benzoylamino)-methyl]-3-hydroxy-piperidine-1-carboxylic acid benzyl ester	475.3
261.		1H-Pyrrole-3-carboxylic acid [1-(3-p-tolyl-propionyl)-piperidin-4-ylmethyl]-amide	354.3
262.		4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 5-methyl-thiophen-2-ylmethyl ester	362.2
263.		3-Hydroxy-4-[(4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester	385.2
264.		4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid cyclopropylmethyl ester	306.2
265.		4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid cyclopentylmethyl ester	334.2
266.		4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 2,5-dimethyl-thiophen-3-yl methyl ester	376.1
267.		1H-Pyrrole-3-carboxylic acid [1-(4-chloro-benzyl)-piperidin-4-ylmethyl]-amide	332.2

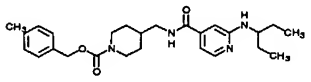
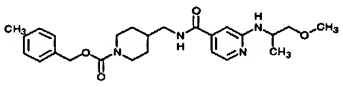
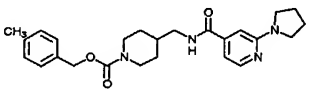
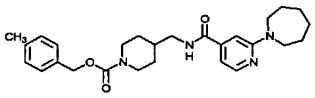
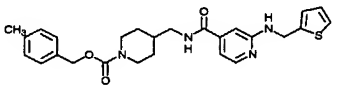
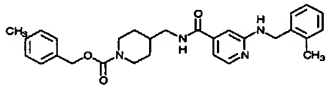
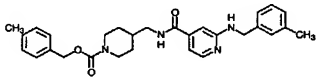
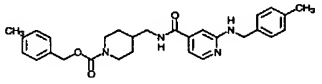
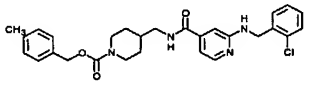
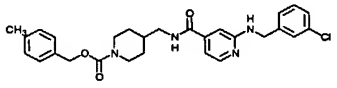
EX.	Structure	Name	MS (M^++1)
268.		1H-Pyrrole-3-carboxylic acid [1-(5-methyl-thiophen-2-ylmethyl)-piperidin-4-ylmethyl]-amide	318.2
269.		1H-Pyrrole-3-carboxylic acid [1-(3-fluoro-benzyl)-piperidin-4-ylmethyl]-amide	316.2
270.		1H-Pyrrole-3-carboxylic acid [1-(2,5-dimethyl-thiophen-3-ylmethyl)-piperidin-4-ylmethyl]-amide	332.2
271.		4-{[(1-Methyl-1H-pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-fluoro-benzyl ester	374.2
272.		4-Hydroxy-N-[1-(2,4,6-trimethyl-benzenesulfonyl)-piperidin-4-ylmethyl]-benzamide	416.2
273.		4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid bicyclo[2.2.1]hept-2-ylmethyl ester	360.2
274.		4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 2-methyl-cyclopropylmethyl ester	320.2
275.		N-[1-(4-Fluoro-benzyl)-piperidin-4-ylmethyl]-4-hydroxy-benzamide	343.2
276.		N-[1-(4-Chloro-benzyl)-piperidin-4-ylmethyl]-4-hydroxy-benzamide	359.1

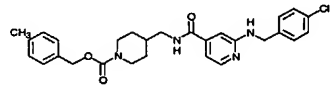
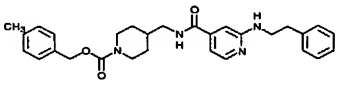
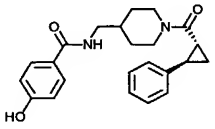
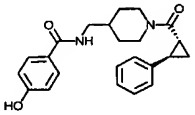
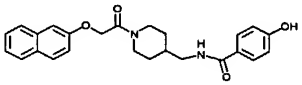
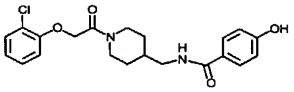
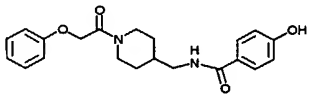
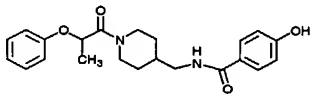
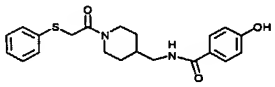
EX.	Structure	Name	MS (M^++1)
277.		4-Hydroxy-N-[1-(1H-pyrrol-2-ylmethyl)-piperidin-4-ylmethyl]-benzamide	314.2
278.		4-Hydroxy-N-[1-(5-methyl-thiophen-2-ylmethyl)-piperidin-4-ylmethyl]-benzamide	345.2
279.		4-Fluoro-4-{[(1H-pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	374.2
280.		4-Fluoro-4-{[(2H-pyrazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	375.2
281.		4-Fluoro-4-{[(1H-pyrazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	375.2
282.		4-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid 5-methyl-thiophen-2-ylmethyl ester	411.2
283.		4-Fluoro-4-[(4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid 4-methyl-benzyl ester	401.2

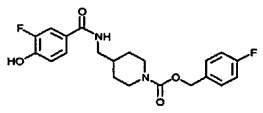
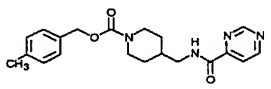
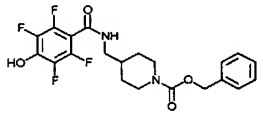
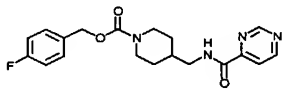
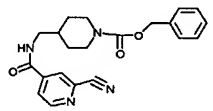
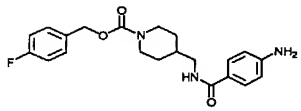
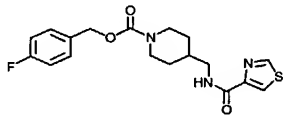
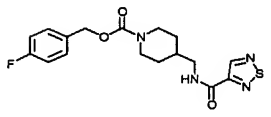
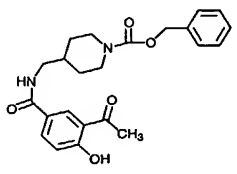
EX.	Structure	Name	MS (M^++1)
284.		4-Fluoro-4-[(4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid 4-chloro-benzyl ester	421.2
285.		4-{[(1H-Pyrazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 5-methyl-thiophen-2-ylmethyl ester	363.1
286.		4-Hydroxy-N-[3-hydroxy-1-(3-phenyl-propyl)-piperidin-4-ylmethyl]-benzamide	369.2
287.		4-Hydroxy-N-[3-hydroxy-1-(4-methyl-benzyl)-piperidin-4-ylmethyl]-benzamide	355.2
288.		4-Hydroxy-N-[3-hydroxy-1-(5-methyl-thiophen-2-ylmethyl)-piperidin-4-ylmethyl]-benzamide	361.1
289.		4-Hydroxy-N-[1-(2-p-tolyloxy-acetyl)-piperidin-4-ylmethyl]-benzamide	383.2

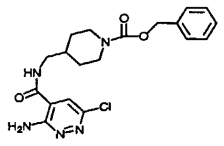
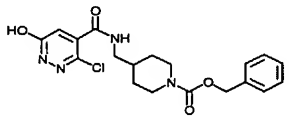
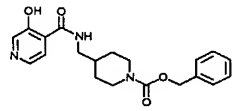
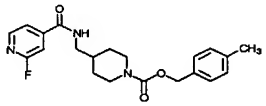
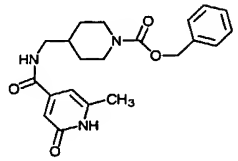
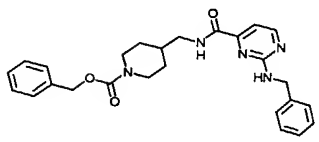
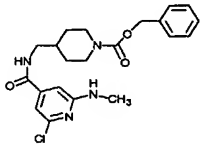
EX.	Structure	Name	MS (M^++1)
290.		4-{[(2-Amino-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	383.2
291.		N-{1-[2-(4-Chloro-phenoxy)-acetyl]-piperidin-4-ylmethyl}-4-hydroxy-benzamide	403.2
292.		N-{1-[2-(4-Fluoro-phenoxy)-acetyl]-piperidin-4-ylmethyl}-4-hydroxy-benzamide	387.3
293.		4-{[(2-Methylamino-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	397.2
294.		4-{[(2-Dimethylamino-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	411.3
295.		4-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-chloro-benzyl ester	376.3
296.		4-{[(2-Benzylamino-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	473.3
297.		4-{[(2-Pentylamino-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	453.4
298.		4-({[2-(2-Fluoro-benzylamino)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid 4-methyl-benzyl ester	491.3

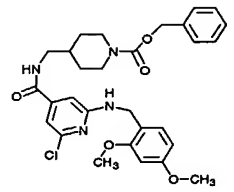
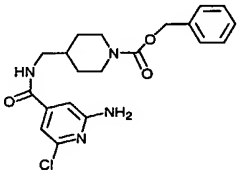
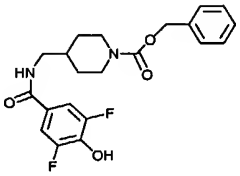
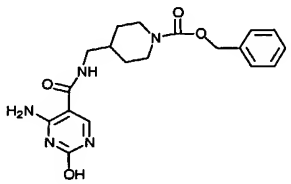
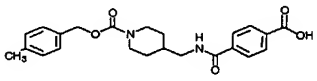
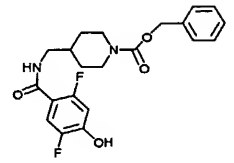
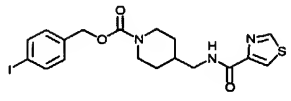
EX.	Structure	Name	MS (M^++1)
299.		4-({[2-(3-Fluoro-benzylamino)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid 4-methyl-benzyl ester	491.3
300.		4-({[2-(4-Fluoro-benzylamino)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid 4-methyl-benzyl ester	491.3
301.		4-Fluoro-4-{[(1H-pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-fluoro-benzyl ester	378.2
302.		4-{[(2-Propylamino-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	425.3
303.		4-{[(2-Butylamino-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	439.3
304.		4-{[(2-Isobutylamino-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	439.3
305.		4-{[(2-Cyclobutylamino-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	437.3
306.		4-{[(2-Cyclopentylamino-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	451.3
307.		4-{[(2-Cyclohexylamino-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	465.3
308.		4-({[2-(Cyclohexyl-methyl-amino)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid 4-methyl-benzyl ester	479.3

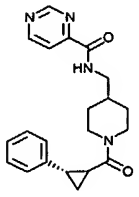
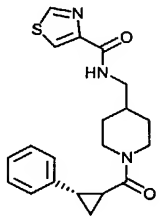
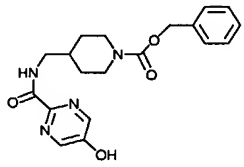
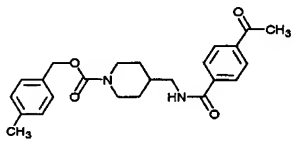
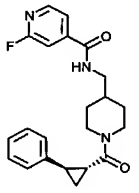
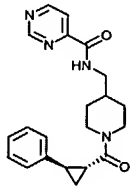
EX.	Structure	Name	MS (M^++1)
309.		4-({[2-(1-Ethyl-propylamino)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid 4-methyl-benzyl ester	453.3
310.		4-({[2-(2-Methoxy-1-methyl-ethylamino)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid 4-methyl-benzyl ester	455.3
311.		4-{[(2-Pyrrolidin-1-yl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	437.3
312.		4-{[(2-Azepan-1-yl-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	465.3
313.		4-[({2-[(Thiophen-2-ylmethyl)-amino]-pyridine-4-carbonyl}-amino)-methyl]-piperidine-1-carboxylic acid 4-methyl-benzyl ester	479.2
314.		4-({[2-(2-Methyl-benzylamino)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid 4-methyl-benzyl ester	487.3
315.		4-({[2-(3-Methyl-benzylamino)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid 4-methyl-benzyl ester	487.3
316.		4-({[2-(4-Methyl-benzylamino)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid 4-methyl-benzyl ester	487.3
317.		4-({[2-(2-Chloro-benzylamino)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid 4-methyl-benzyl ester	507.3
318.		4-({[2-(3-Chloro-benzylamino)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid 4-methyl-benzyl ester	507.3

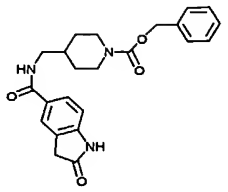
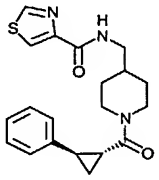
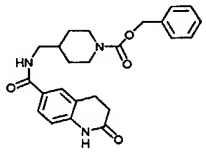
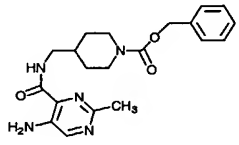
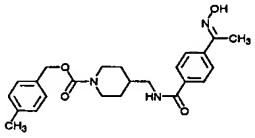
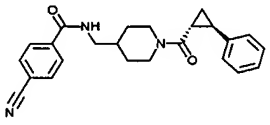
EX.	Structure	Name	MS (M^++1)
319.		4-({[2-(4-Chloro-benzylamino)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid 4-methyl-benzyl ester	507.3
320.		4-{[(2-Phenethylamino-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	487.3
321.		4-Hydroxy-N-[1-(2-phenyl-cyclopropanecarbonyl)-piperidin-4-ylmethyl]-benzamide	379.3
322.		4-Hydroxy-N-[1-(2-phenyl-cyclopropanecarbonyl)-piperidin-4-ylmethyl]-benzamide	379.3
323.		4-Hydroxy-N-{1-[2-(naphthalen-2-yloxy)-acetyl]-piperidin-4-ylmethyl}-benzamide	419.4
324.		N-{1-[2-(2-Chloro-phenoxy)-acetyl]-piperidin-4-ylmethyl}-4-hydroxy-benzamide	403.3
325.		4-Hydroxy-N-[1-(2-phenoxy-acetyl)-piperidin-4-ylmethyl]-benzamide	369.4
326.		4-Hydroxy-N-[1-(2-phenoxy-propionyl)-piperidin-4-ylmethyl]-benzamide	383.4
327.		4-Hydroxy-N-[1-(2-phenylsulfanyl-acetyl)-piperidin-4-ylmethyl]-benzamide	385.3

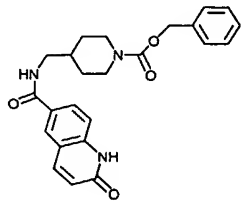
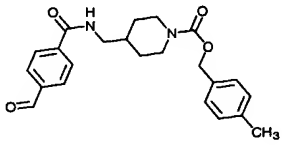
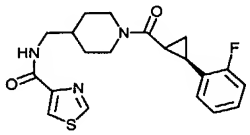
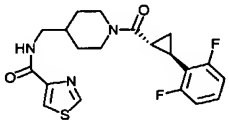
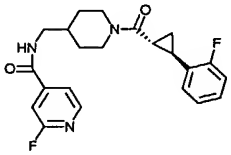
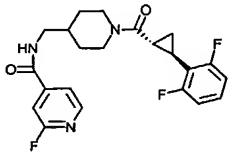
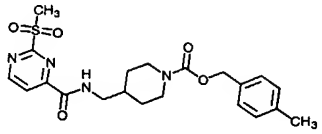
EX.	Structure	Name	MS (M^++1)
328.		4-[(3-Fluoro-4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid 4-fluoro-benzyl ester	405.3
329.		4-{[(Pyrimidine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	369.4
330.		4-[(2,3,5,6-Tetrafluoro-4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester	441.3
331.		4-{[(Pyrimidine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-fluoro-benzyl ester	373.4
332.		4-{[(2-Cyano-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	379.4
333.		4-[(4-Amino-benzoylamino)-methyl]-piperidine-1-carboxylic acid 4-fluoro-benzyl ester	386.4
334.		4-{[(Thiazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-fluoro-benzyl ester	378.4
335.		4-{[([1,2,5]Thiadiazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-fluoro-benzyl ester	379.4
336.		4-[(3-Acetyl-4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester	411.4

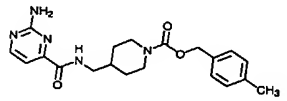
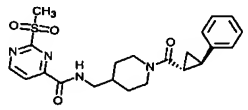
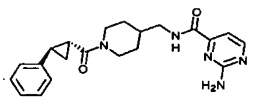
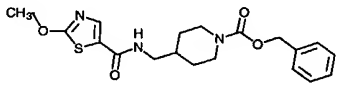
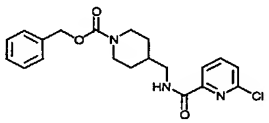
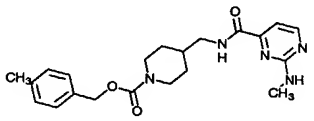
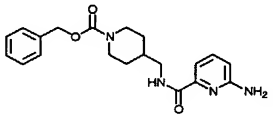
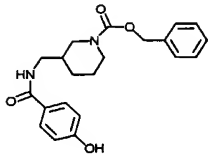
EX.	Structure	Name	MS (M^++1)
337.		4-{[(3-Amino-6-chloro-pyridazine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	404.4
338.		4-{[(3-Chloro-6-hydroxy-pyridazine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	405.3
339.		4-{[(3-Hydroxy-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	370.4
340.		4-{[(2-Fluoro-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	386.4
341.		4-{[(6-Methyl-2-oxo-1,2-dihydro-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	384.4
342.		4-{[(2-Benzylamino-pyrimidine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	460.4
343.		4-{[(2-Chloro-6-methylamino-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	417.4

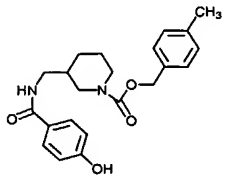
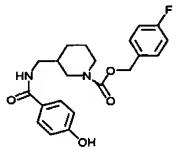
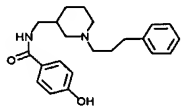
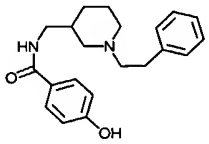
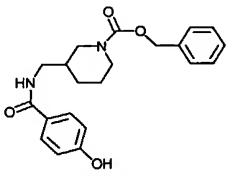
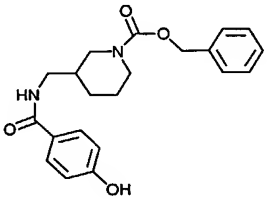
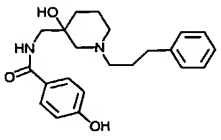
EX.	Structure	Name	MS (M^++1)
344.		4-({[2-Chloro-6-(2,4-dimethoxy-benzylamino)-pyridine-4-carbonyl]-amino}-methyl)-piperidine-1-carboxylic acid benzyl ester	553.5
345.		4-{[(2-Amino-6-chloro-pyridine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	403.4
346.		4-[(3,5-Difluoro-4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester	405.4
347.		4-{[(4-Amino-2-hydroxy-pyrimidine-5-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	386.4
348.		4-[(4-Carboxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid 4-methyl-benzyl ester	411.4
349.		4-[(2,5-Difluoro-4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester	405.4
350.		4-{[(Thiazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-iodo-benzyl ester	486.3

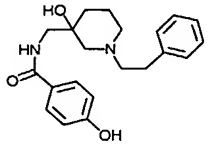
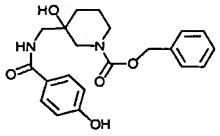
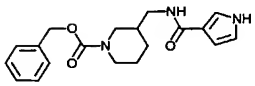
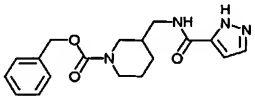
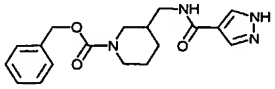
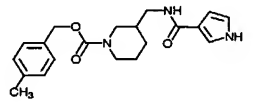
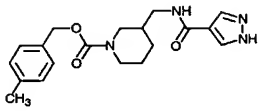
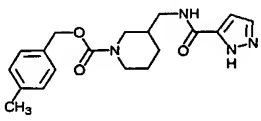
EX.	Structure	Name	MS (M^++1)
351.		Pyrimidine-4-carboxylic acid [1-(2-phenyl-cyclopropanecarbonyl)-piperidin-4-ylmethyl]-amide	365.4
352.		Thiazole-4-carboxylic acid [1-(2-phenyl-cyclopropanecarbonyl)-piperidin-4-ylmethyl]-amide	370.4
353.		4-{[(5-Hydroxy-pyrimidine-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	371.4
354.		4-[(4-Acetyl-benzoylamino)-methyl]-piperidine-1-carboxylic acid 4-methyl-benzyl ester	409.3
355.		2-Fluoro-N-[1-(2-phenyl-cyclopropanecarbonyl)-piperidin-4-ylmethyl]-isonicotinamide	382.4
356.		Pyrimidine-4-carboxylic acid [1-(2-phenyl-cyclopropanecarbonyl)-piperidin-4-ylmethyl]-amide	365.4

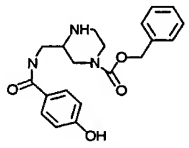
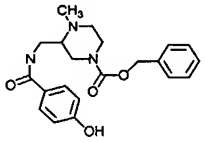
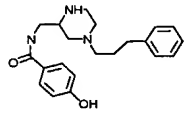
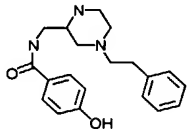
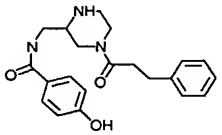
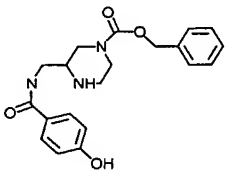
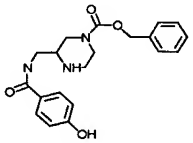
EX.	Structure	Name	MS (M^++1)
357.		4-{[(2-Oxo-2,3-dihydro-1H-indole-5-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	408.3
358.		Thiazole-4-carboxylic acid [1-(2-phenyl-cyclopropanecarbonyl)-piperidin-4-ylmethyl]-amide	370.3
359.		4-{[(2-Oxo-1,2,3,4-tetrahydro-quinoline-6-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	422.4
360.		4-{[(5-Amino-2-methyl-pyrimidine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	384.4
361.		4-{[4-(1-Hydroxyimino-ethyl)-benzoylamino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	424.3
362.		4-Cyano-N-[1-(2-phenyl-cyclopropanecarbonyl)-piperidin-4-ylmethyl]-benzamide	388.3

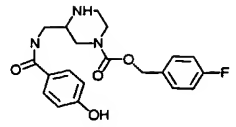
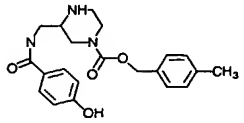
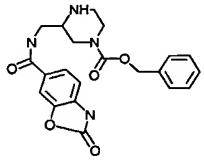
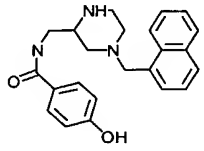
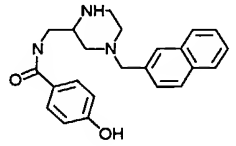
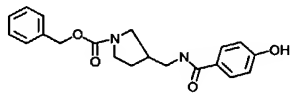
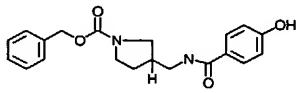
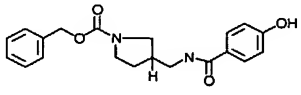
EX.	Structure	Name	MS (M^++1)
363.		4-{[(2-Oxo-1,2-dihydro-quinoline-6-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	420.3
364.		4-[(4-Formyl-benzoylamino)-methyl]-piperidine-1-carboxylic acid 4-methyl-benzyl ester	395.3
365.		Thiazole-4-carboxylic acid {1-[2-(2-fluoro-phenyl)-cyclopropanecarbonyl]-piperidin-4-ylmethyl}-amide	388.2
366.		Thiazole-4-carboxylic acid {1-[2-(2,6-difluoro-phenyl)-cyclopropanecarbonyl]-piperidin-4-ylmethyl}-amide	406.2
367.		2-Fluoro-N-{1-[2-(2-fluoro-phenyl)-cyclopropanecarbonyl]-piperidin-4-ylmethyl}-isonicotinamide	400.3
368.		N-{1-[2-(2,6-Difluoro-phenyl)-cyclopropanecarbonyl]-piperidin-4-ylmethyl}-2-fluoro-isonicotinamide	418.3
369.		4-{[(2-Methanesulfonyl-pyrimidine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	448.2

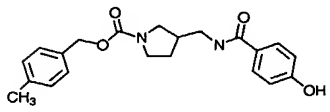
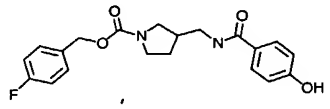
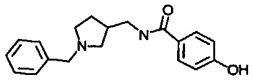
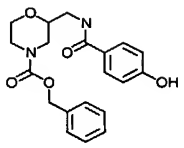
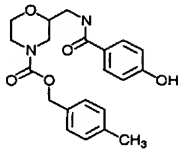
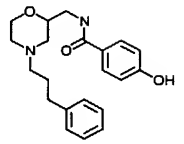
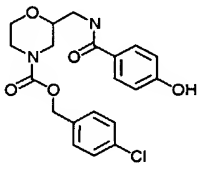
EX.	Structure	Name	MS (M^++1)
370.		4-{[(2-Amino-pyrimidine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	384.3
371.		2-Methanesulfonyl-pyrimidine-4-carboxylic acid [1-(2-phenyl-cyclopropanecarbonyl)-piperidin-4-ylmethyl]-amide	443.3
372.		2-Amino-pyrimidine-4-carboxylic acid [1-(2-phenyl-cyclopropanecarbonyl)-piperidin-4-ylmethyl]-amide	380.2
373.		4-{[(2-Ethoxy-thiazole-5-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	404.2
374.		4-{[(6-Chloro-pyridine-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	388.2
375.		4-{[(2-Methylamino-pyrimidine-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	398.3
376.		4-{[(6-Amino-pyridine-2-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	369.2
377.		3-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester	369.2

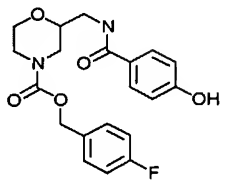
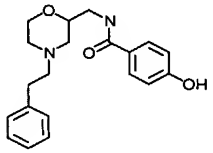
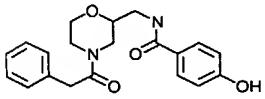
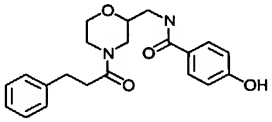
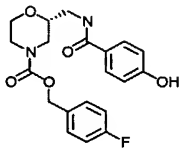
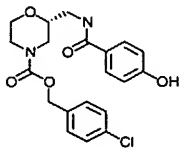
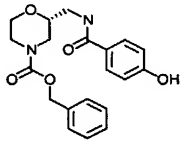
EX.	Structure	Name	MS (M^++1)
378.		3-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid 4-methyl-benzyl ester	383.3
379.		3-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid 4-fluoro-benzyl ester	387.2
380.		4-Hydroxy-N-[1-(3-phenyl-propyl)-piperidin-3-ylmethyl]-benzamide	353.3
381.		4-Hydroxy-N-(1-phenethyl-piperidin-3-ylmethyl)-benzamide	339.3
382.		3-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester	369.3
383.		3-[(4-Hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester	369.3
384.		4-Hydroxy-N-[3-hydroxy-1-(3-phenyl-propyl)-piperidin-3-ylmethyl]-benzamide	369.3

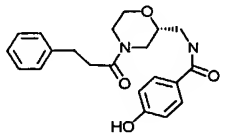
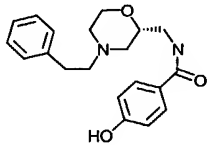
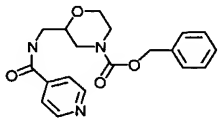
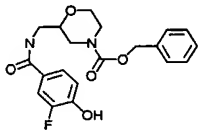
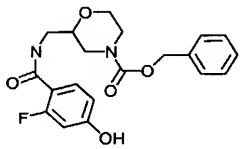
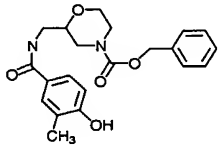
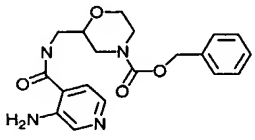
EX.	Structure	Name	MS (M^++1)
385.		4-Hydroxy-N-(3-hydroxy-1-phenethyl-piperidin-3-ylmethyl)-benzamide	355.2
386.		3-Hydroxy-3-[(4-hydroxy-benzoylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester	385.2
387.		3-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	342.7
388.		3-{[(2H-Pyrazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	343.2
389.		3-{[(1H-Pyrazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester	343.2
390.		3-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	356.2
391.		3-{[(1H-Pyrazole-4-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	357.2
392.		3-{[(2H-Pyrazole-3-carbonyl)-amino]-methyl}-piperidine-1-carboxylic acid 4-methyl-benzyl ester	357.2

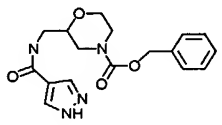
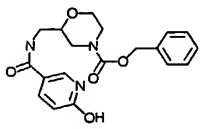
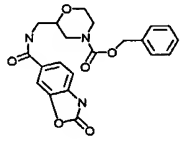
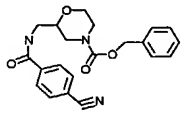
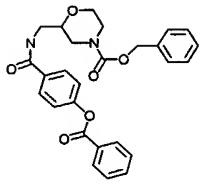
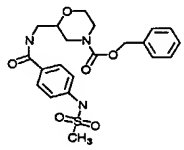
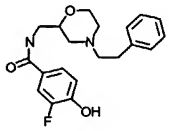
EX.	Structure	Name	MS (M^++1)
393.		3-[(4-Hydroxy-benzoylamino)-methyl]-piperazine-1-carboxylic acid benzyl ester	370.2
394.		3-[(4-Hydroxy-benzoylamino)-methyl]-4-methyl-piperazine-1-carboxylic acid benzyl ester	384.3
395.		4-Hydroxy-N-[4-(3-phenyl-propyl)-piperazin-2-ylmethyl]-benzamide	354.2
396.		4-Hydroxy-N-(4-phenethyl-piperazin-2-ylmethyl)-benzamide	340.3
397.		4-Hydroxy-N-[4-(3-phenyl-propionyl)-piperazin-2-ylmethyl]-benzamide	368.3
398.		3-[(4-Hydroxy-benzoylamino)-methyl]-piperazine-1-carboxylic acid benzyl ester	370.2
399.		3-[(4-Hydroxy-benzoylamino)-methyl]-piperazine-1-carboxylic acid benzyl ester	370.2

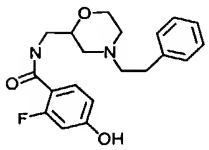
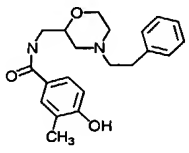
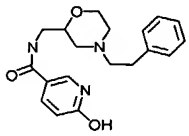
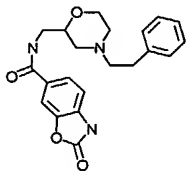
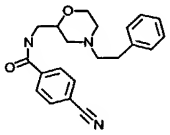
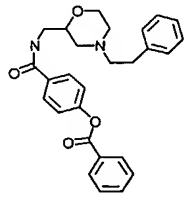
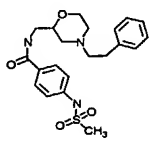
EX.	Structure	Name	MS (M^++1)
400.		3-[(4-Hydroxy-benzoylamino)-methyl]-piperazine-1-carboxylic acid 4-fluoro-benzyl ester	388.2
401.		3-[(4-Hydroxy-benzoylamino)-methyl]-piperazine-1-carboxylic acid 4-methyl-benzyl ester	384.2
402.		3-{[(2-Oxo-2,3-dihydro-benzooxazole-6-carbonyl)-amino]-methyl}-piperazine-1-carboxylic acid benzyl ester	411.2
403.		4-Hydroxy-N-(4-naphthalen-1-ylmethyl-piperazin-2-ylmethyl)-benzamide	368.4
404.		4-Hydroxy-N-(4-naphthalen-2-ylmethyl-piperazin-2-ylmethyl)-benzamide	354.2
405.		3-[(4-Hydroxy-benzoylamino)-methyl]-pyrrolidine-1-carboxylic acid benzyl ester	376.3
406.		3-[(4-Hydroxy-benzoylamino)-methyl]-pyrrolidine-1-carboxylic acid benzyl ester	376.3
407.		3-[(4-Hydroxy-benzoylamino)-methyl]-pyrrolidine-1-carboxylic acid benzyl ester	355.3

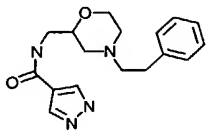
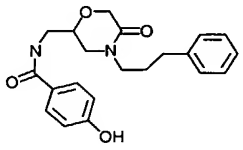
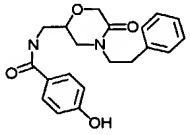
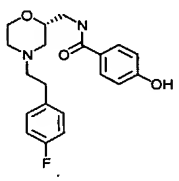
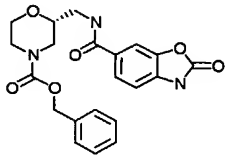
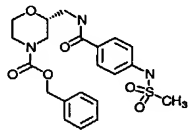
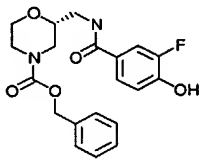
EX.	Structure	Name	MS (M^++1)
408.		3-[(4-Hydroxy-benzoylamino)-methyl]-pyrrolidine-1-carboxylic acid 4-methyl-benzyl ester	369.3
409.		3-[(4-Hydroxy-benzoylamino)-methyl]-pyrrolidine-1-carboxylic acid 4-fluoro-benzyl ester	373.3
410.		N-(1-Benzyl-pyrrolidin-3-ylmethyl)-4-hydroxy-benzamide	311.4
411.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid benzyl ester	371.2
412.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-methyl-benzyl ester	385.7
413.		4-Hydroxy-N-[4-(3-phenyl-propyl)-morpholin-2-ylmethyl]-benzamide	355.2
414.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-chloro-benzyl ester	405.1

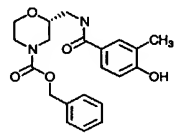
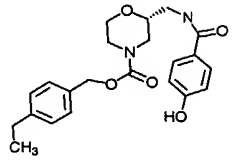
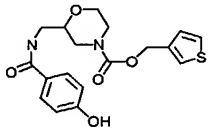
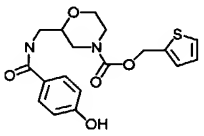
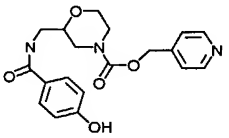
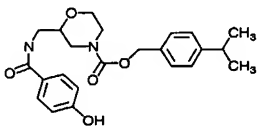
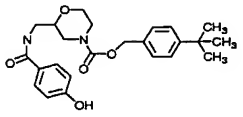
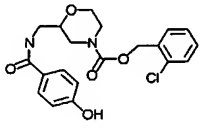
EX.	Structure	Name	MS (M^++1)
415.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-fluoro-benzyl ester	389.1
416.		4-Hydroxy-N-(4-phenethyl-morpholin-2-ylmethyl)-benzamide	341.1
417.		4-Hydroxy-N-(4-phenylacetyl-morpholin-2-ylmethyl)-benzamide	355.2
418.		4-Hydroxy-N-[4-(3-phenyl-propionyl)-morpholin-2-ylmethyl]-benzamide	369.2
419.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-fluoro-benzyl ester	389.3
420.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-chloro-benzyl ester	405.1
421.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid benzyl ester	371.1

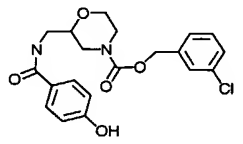
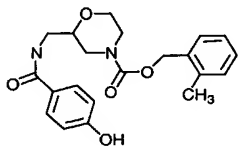
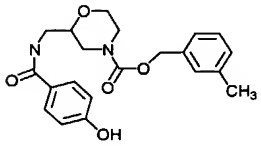
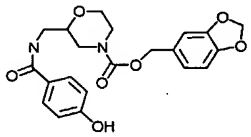
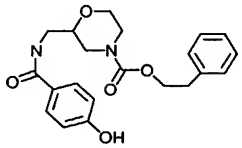
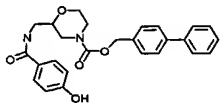
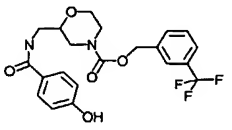
EX.	Structure	Name	MS (M^++1)
422.		4-Hydroxy-N-[4-(3-phenyl-propionyl)-morpholin-2-ylmethyl]-benzamide	369.2
423.		4-Hydroxy-N-(4-phenethyl-morpholin-2-ylmethyl)-benzamide	341.2
424.		2-{[(Pyridine-4-carbonyl)-amino]-methyl}-morpholine-4-carboxylic acid benzyl ester	56.2
425.		2-[(3-Fluoro-4-hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid benzyl ester	389.1
426.		2-[(2-Fluoro-4-hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid benzyl ester	389.1
427.		2-[(4-Hydroxy-3-methyl-benzoylamino)-methyl]-morpholine-4-carboxylic acid benzyl ester	385.2
428.		2-{[(3-Amino-pyridine-4-carbonyl)-amino]-methyl}-morpholine-4-carboxylic acid benzyl ester	371.1

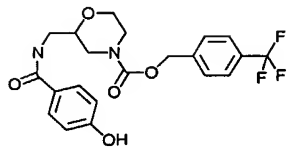
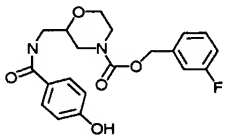
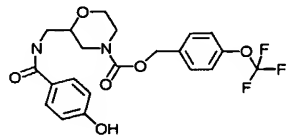
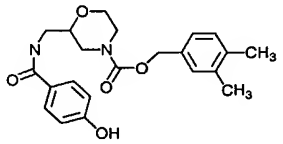
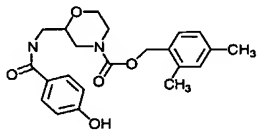
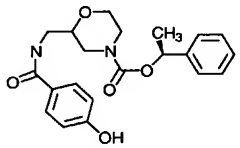
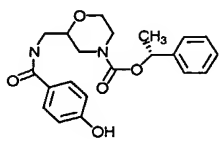
EX.	Structure	Name	MS (M^++1)
429.		2-{[(1H-Pyrazole-4-carbonyl)-amino]-methyl}-morpholine-4-carboxylic acid benzyl ester	345.2
430.		2-{[(6-Hydroxy-pyridine-3-carbonyl)-amino]-methyl}-morpholine-4-carboxylic acid benzyl ester	372.2
431.		2-{[(2-Oxo-2,3-dihydro-benzooxazole-6-carbonyl)-amino]-methyl}-morpholine-4-carboxylic acid benzyl ester	412.1
432.		2-[(4-Cyano-benzoylamino)-methyl]-morpholine-4-carboxylic acid benzyl ester	380.2
433.		2-[(4-Benzoyloxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid benzyl ester	475.2
434.		2-[(4-Methanesulfonylamino-benzoylamino)-methyl]-morpholine-4-carboxylic acid benzyl ester	448.1
435.		3-Fluoro-4-hydroxy-N-(4-phenethyl-morpholin-2-ylmethyl)-benzamide	359.2

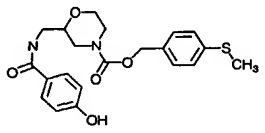
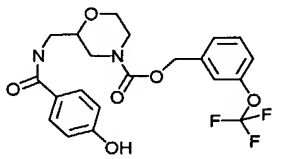
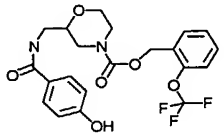
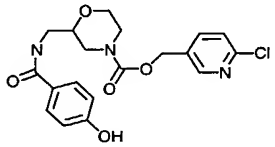
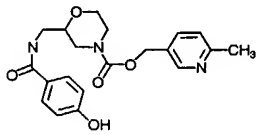
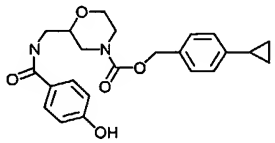
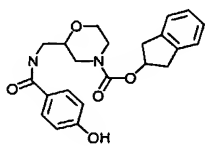
EX.	Structure	Name	MS (M^++1)
436.		2-Fluoro-4-hydroxy-N-(4-phenethyl-morpholin-2-ylmethyl)-benzamide	359.1
437.		4-Hydroxy-3-methyl-N-(4-phenethyl-morpholin-2-ylmethyl)-benzamide	355.2
438.		6-Hydroxy-N-(4-phenethyl-morpholin-2-ylmethyl)-nicotinamide	342.2
439.		2-Oxo-2,3-dihydro-benzooxazole-6-carboxylic acid (4-phenethyl-morpholin-2-ylmethyl)-amide	382.1
440.		4-Cyano-N-(4-phenethyl-morpholin-2-ylmethyl)-benzamide	350.2
441.		Benzoic acid 4-[(4-phenethyl-morpholin-2-ylmethyl)-carbamoyl]-phenyl ester	445.2
442.		4-Methanesulfonylamino-N-(4-phenethyl-morpholin-2-ylmethyl)-benzamide	418.1

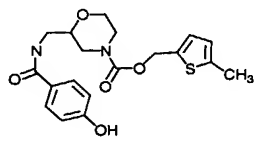
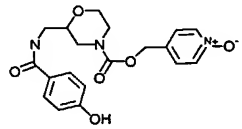
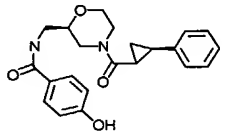
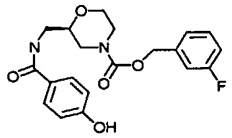
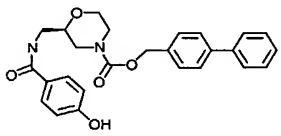
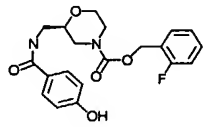
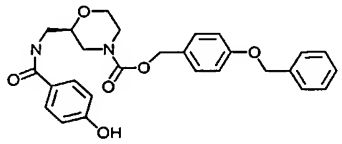
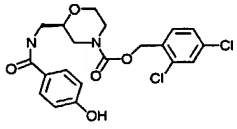
EX.	Structure	Name	MS (M^++1)
443.		1H-Pyrazole-4-carboxylic acid (4-phenethyl-morpholin-2-ylmethyl)-amide	341.2
444.		4-Hydroxy-N-[5-oxo-4-(3-phenyl-propyl)-morpholin-2-ylmethyl]-benzamide	369.7
445.		4-Hydroxy-N-(5-oxo-4-phenethyl-morpholin-2-ylmethyl)-benzamide	355.6
446.		N-{4-[2-(4-Fluoro-phenyl)-ethyl]-morpholin-2-ylmethyl}-4-hydroxy-benzamide	359.3
447.		2-{[(2-Oxo-2,3-dihydro-benzooxazole-6-carbonyl)-amino]-methyl}-morpholine-4-carboxylic acid benzyl ester	412.3
448.		2-[(4-Methanesulfonylamino-benzoylamino)-methyl]-morpholine-4-carboxylic acid benzyl ester	448.3
449.		2-[(3-Fluoro-4-hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid benzyl ester	389.3

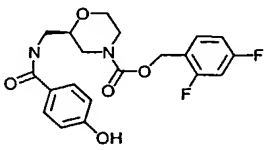
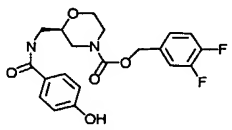
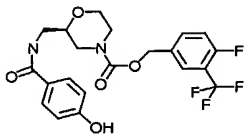
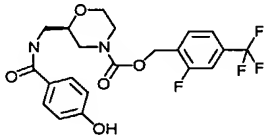
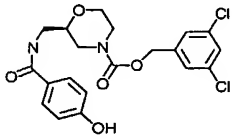
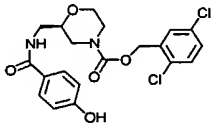
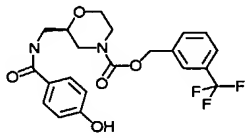
EX.	Structure	Name	MS (M^++1)
450.		2-[(4-Hydroxy-3-methyl-benzoylamino)-methyl]-morpholine-4-carboxylic acid benzyl ester	385.3
451.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-ethyl-benzyl ester	399.4
452.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid thiophen-3-ylmethyl ester	377.2
453.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid thiophen-2-ylmethyl ester	377.2
454.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid pyridin-4-ylmethyl ester	372.2
455.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-isopropyl-benzyl ester	413.3
456.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-tert-butyl-benzyl ester	427.3
457.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 2-chloro-benzyl ester	405.2

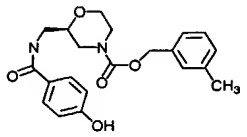
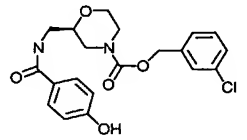
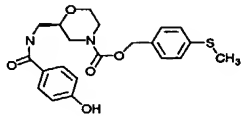
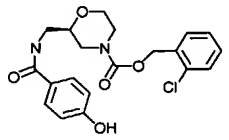
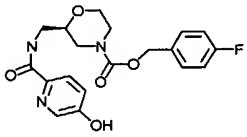
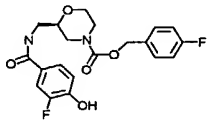
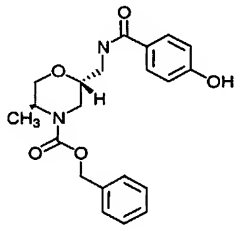
EX.	Structure	Name	MS (M^++1)
458.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 3-chloro-benzyl ester	405.2
459.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 2-methyl-benzyl ester	385.3
460.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 3-methyl-benzyl ester	385.3
461.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid benzo[1,3]dioxol-5-ylmethyl ester	415.3
462.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid phenethyl ester	385.3
463.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid biphenyl-4-ylmethyl ester	447.3
464.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 3-trifluoromethyl-benzyl ester	439.3

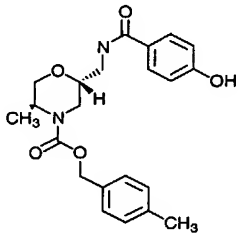
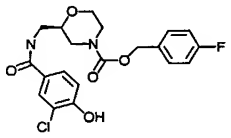
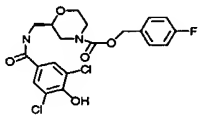
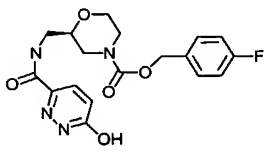
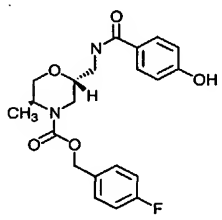
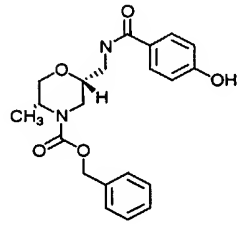
EX.	Structure	Name	MS (M^++1)
465.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-trifluoromethyl-benzyl ester	439.3
466.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 3-fluoro-benzyl ester	389.3
467.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-trifluoromethoxy-benzyl ester	455.3
468.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 3,4-dimethyl-benzyl ester	399.3
469.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 2,4-dimethyl-benzyl ester	399.3
470.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 1-phenyl-ethyl ester	385.3
471.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 1-phenyl-ethyl ester	385.3

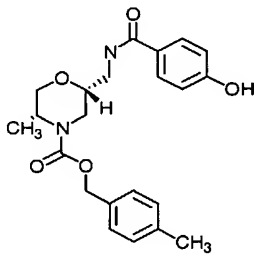
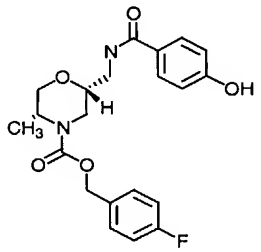
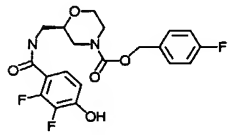
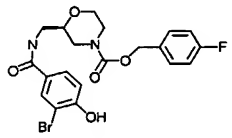
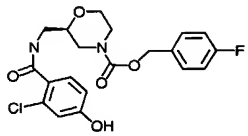
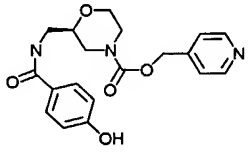
EX.	Structure	Name	MS (M^++1)
472.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-methylsulfanyl-benzyl ester	417.3
473.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 3-trifluoromethoxy-benzyl ester	455.3
474.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 2-trifluoromethoxy-benzyl ester	455.3
475.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 6-chloro-pyridin-3-ylmethyl ester	406.2
476.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 6-methyl-pyridin-3-ylmethyl ester	386.3
477.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-cyclopropyl-benzyl ester	411.3
478.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid indan-2-yl ester	397.3

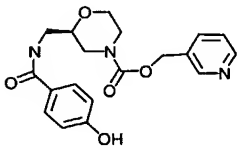
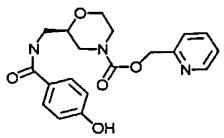
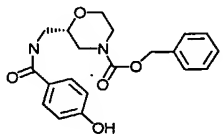
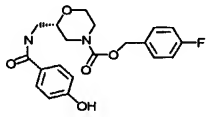
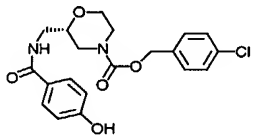
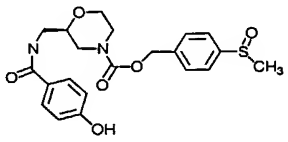
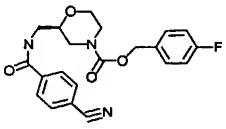
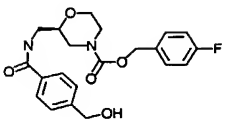
EX.	Structure	Name	MS (M^++1)
479.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 5-methyl-thiophen-2-ylmethyl ester	391.3
480.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 1-oxy-pyridin-4-ylmethyl ester	388.2
481.		4-Hydroxy-N-[4-(2-phenyl-cyclopropanecarbonyl)-morpholin-2-ylmethyl]-benzamide	381.3
482.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 3-fluoro-benzyl ester	389.4
483.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid biphenyl-4-ylmethyl ester	447.4
484.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 2-fluoro-benzyl ester	389.4
485.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-benzyloxy-benzyl ester	477.25
486.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 2,4-dichloro-benzyl ester	439.3

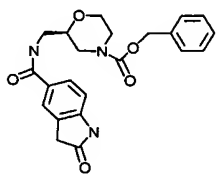
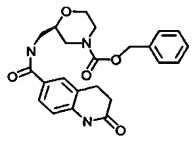
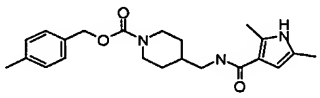
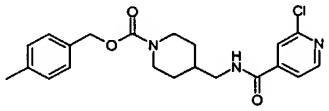
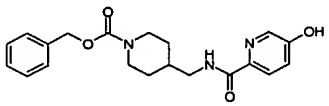
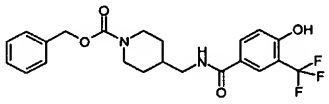
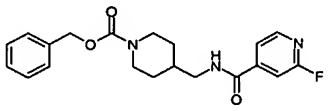
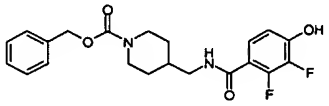
EX.	Structure	Name	MS (M^++1)
487.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 2,4-difluoro-benzyl ester	407.4
488.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 3,4-difluoro-benzyl ester	407.4
489.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-fluoro-3-trifluoromethyl-benzyl ester	457.4
490.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 2-fluoro-4-trifluoromethyl-benzyl ester	457.4
491.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 3,5-dichloro-benzyl ester	439.3
492.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 2,5-dichloro-benzyl ester	439.3
493.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 3-trifluoromethyl-benzyl ester	439.4

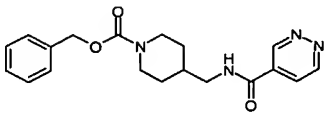
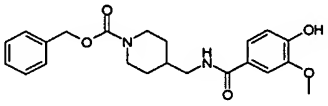
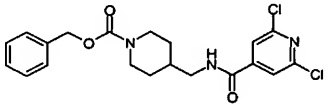
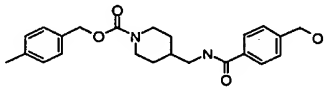
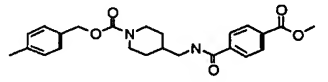
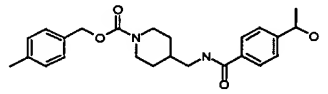
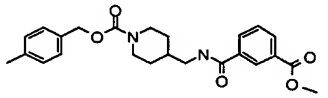
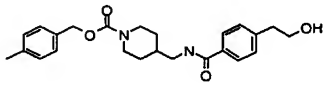
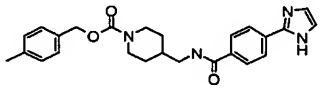
EX.	Structure	Name	MS (M^++1)
494.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 3-methyl-benzyl ester	385.4
495.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 3-chloro-benzyl ester	405.3
496.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-methylsulfanyl-benzyl ester	417.3
497.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 2-chloro-benzyl ester	405.3
498.		2-{[(5-Hydroxy-pyridine-2-carbonyl)-amino]-methyl}-morpholine-4-carboxylic acid 4-fluoro-benzyl ester	390.3
499.		2-[(3-Fluoro-4-hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-fluoro-benzyl ester	407.3
500.		2-[(4-Hydroxy-benzoylamino)-methyl]-5-methyl-morpholine-4-carboxylic acid benzyl ester	385.4

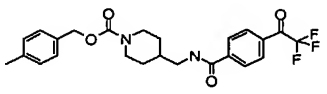
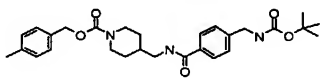
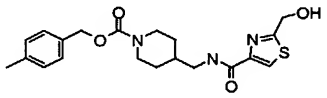
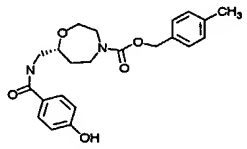
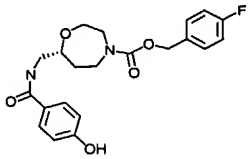
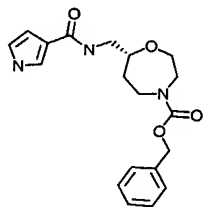
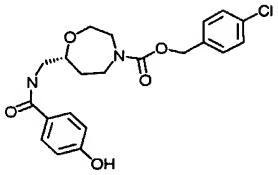
EX.	Structure	Name	MS (M^++1)
501.		2-[(4-Hydroxy-benzoylamino)-methyl]-5-methyl-morpholine-4-carboxylic acid 4-methyl-benzyl ester	399.3
502.		2-[(3-Chloro-4-hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-fluoro-benzyl ester	423.3
503.		2-[(3,5-Dichloro-4-hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-fluoro-benzyl ester	457.2
504.		2-{[(6-Hydroxy-pyridazine-3-carbonyl)-amino]-methyl}-morpholine-4-carboxylic acid 4-fluoro-benzyl ester	391.4
505.		2-[(4-Hydroxy-benzoylamino)-methyl]-5-methyl-morpholine-4-carboxylic acid 4-fluoro-benzyl ester	403.4
506.		2-[(4-Hydroxy-benzoylamino)-methyl]-5-methyl-morpholine-4-carboxylic acid benzyl ester	385.3

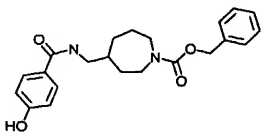
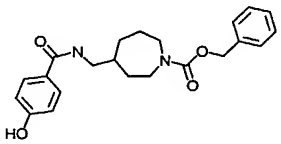
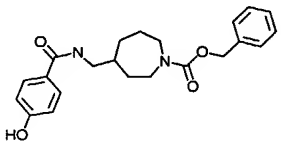
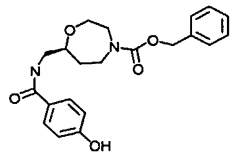
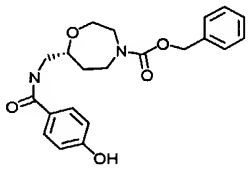
EX.	Structure	Name	MS (M^++1)
507.		2-[(4-Hydroxy-benzoylamino)-methyl]-5-methyl-morpholine-4-carboxylic acid 4-methyl-benzyl ester	399.4
508.		2-[(4-Hydroxy-benzoylamino)-methyl]-5-methyl-morpholine-4-carboxylic acid 4-fluoro-benzyl ester	403.3
509.		2-[(2,3-Difluoro-4-hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-fluoro-benzyl ester	425.2
510.		2-[(3-Bromo-4-hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-fluoro-benzyl ester	467.2
511.		2-[(2-Chloro-4-hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-fluoro-benzyl ester	423.2
512.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid pyridin-4-ylmethyl ester	372.3

EX.	Structure	Name	MS (M^++1)
513.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid pyridin-3-ylmethyl ester	372.3
514.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid pyridin-2-ylmethyl ester	372.3
515.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid benzyl ester	371.3
516.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-fluoro-benzyl ester	389.3
517.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-chloro-benzyl ester	405.3
518.		2-[(4-Hydroxy-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-methanesulfinyl-benzyl ester	433.3
519.		2-[(4-Cyano-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-fluoro-benzyl ester	398.4
520.		2-[(4-Hydroxymethyl-benzoylamino)-methyl]-morpholine-4-carboxylic acid 4-fluoro-benzyl ester	403.4

EX.	Structure	Name	MS (M^++1)
521.		2-{[(2-Oxo-2,3-dihydro-1H-indole-5-carbonyl)-amino]-methyl}-morpholine-4-carboxylic acid benzyl ester	410.3
522.		2-{[(2-Oxo-1,2,3,4-tetrahydro-quinoline-6-carbonyl)-amino]-methyl}-morpholine-4-carboxylic acid benzyl ester	424.4
523.		4-Methylbenzyl 4-({[(2,5-dimethyl-1H-pyrrol-3-yl)carbonyl]amino}methyl)piperidine-1-carboxylate	370.2
524.		4-Methylbenzyl 4-{[(2-chloroisonicotinoyl)amino]methyl}piperidine-1-carboxylate	402.1
525.		Benzyl 4-({[(5-hydroxypyridin-2-yl)carbonyl]amino}methyl)piperidine-1-carboxylate	370.3
526.		Benzyl 4-({[4-hydroxy-3-(trifluoromethyl)benzoyl]amino}methyl)piperidine-1-carboxylate	437.4
527.		Benzyl 4-{[(2-fluoroisonicotinoyl)amino]methyl}piperidine-1-carboxylate	372.4
528.		Benzyl 4-{[(2,3-difluoro-4-hydroxybenzoyl)amino]methyl}piperidine-1-carboxylate	405.3

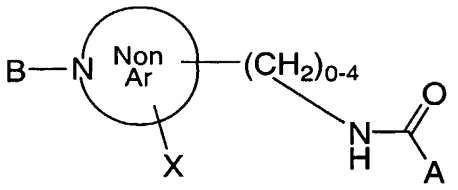
EX.	Structure	Name	MS (M^++1)
529.		Benzyl 4-{[(pyridazin-4-ylcarbonyl)amino]methyl}piperidine-1-carboxylate	355.3
530.		Benzyl 4-{[(4-hydroxy-3-methoxybenzoyl)amino]methyl}piperidine-1-carboxylate	399.4
531.		Benzyl 4-{[(2,6-dichloroisonicotinoyl)amino]methyl}piperidine-1-carboxylate	423.3
532.		4-Methylbenzyl 4-({[4-(hydroxymethyl)benzoyl]amino}methyl)piperidine-1-carboxylate	397.4
533.		4-Methylbenzyl 4-({[4-(methoxycarbonyl)benzoyl]amino}methyl)piperidine-1-carboxylate	425.5
534.		4-Methylbenzyl 4-({[4-(1-hydroxyethyl)benzoyl]amino}methyl)piperidine-1-carboxylate	411.4
535.		4-Methylbenzyl 4-({[3-(methoxycarbonyl)benzoyl]amino}methyl)piperidine-1-carboxylate	425.4
536.		4-Methylbenzyl 4-({[4-(2-hydroxyethyl)benzoyl]amino}methyl)piperidine-1-carboxylate	411.3
537.		4-Methylbenzyl 4-({[4-(1H-imidazol-2-yl)benzoyl]amino}methyl)piperidine-1-carboxylate	433.3

EX.	Structure	Name	MS (M^++1)
538.		4-Methylbenzyl 4-({[4-(trifluoroacetyl)benzoyl]amino}methyl) piperidine-1-carboxylate	481.2
539.		4-Methylbenzyl 4-{[(4-{[(tert-butoxycarbonyl)amino]methyl}benzoyl)amino] methyl}piperidine-1-carboxylate	496.4
540.		4-Methylbenzyl 4-[({[2-(hydroxymethyl)-1,3-thiazol-4-yl]carbonyl}amino)methyl]piperidine-1-carboxylate	404.2
541.		7-[(4-Hydroxy-benzoylamino)-methyl]-[1,4]oxazepane-4-carboxylic acid 4-methyl-benzyl ester	399.4
542.		7-[(4-Hydroxy-benzoylamino)-methyl]-[1,4]oxazepane-4-carboxylic acid 4-fluoro-benzyl ester	403.4
543.		7-{[(1H-Pyrrole-3-carbonyl)-amino]-methyl}-[1,4]oxazepane-4-carboxylic acid benzyl ester	358.3
544.		7-[(4-Hydroxy-benzoylamino)-methyl]-[1,4]oxazepane-4-carboxylic acid 4-chloro-benzyl ester	419.4

EX.	Structure	Name	MS (M^++1)
545.		4-[(4-Hydroxy-benzoylamino)-methyl]-azepane-1-carboxylic acid benzyl ester	383.4
546.		4-[(4-Hydroxy-benzoylamino)-methyl]-azepane-1-carboxylic acid benzyl ester	383.4
547.		4-[(4-Hydroxy-benzoylamino)-methyl]-azepane-1-carboxylic acid benzyl ester	383.4
548.		7-[(4-Hydroxy-benzoylamino)-methyl]-[1,4]oxazepane-4-carboxylic acid benzyl ester	385.4
549.		7-[(4-Hydroxy-benzoylamino)-methyl]-[1,4]oxazepane-4-carboxylic acid benzyl ester	385.4

WHAT IS CLAIMED IS:

1. A compound having the Formula (I):



(I)

or a pharmaceutically acceptable salt thereof, wherein

NonAr is a nonaromatic 5-7 membered ring containing a) 1 nitrogen ring atom, b) 2 nitrogen ring atoms, c) 1 nitrogen and 1 oxygen ring atom, or d) 1 nitrogen and 1 sulfur ring atom, wherein the remaining ring atoms are carbon;

A is a phenyl optionally substituted with 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-7}cycloalkyl, -CF_3, halogen, -OH, –CN, imidazolyl, -C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), -O-C_{1-4}alkyl, -C(O)-C_{0-4}alkyl, -C(O)-O-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkylphenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O-C_{1-4}alkyl, or –$NHSO_2$-C_{1-4}alkyl, -O-C_{1-4}alkylphenyl, or hydroxyiminoethyl; any alkyl optionally substituted with 1-6 –OH or halogen; or

A is pyrrolyl, imidazolyl, pyrazolyl, triazolyl, thiophenyl, thiazolyl, thiadiazolyl, oxazolyl, or isoxazolyl, each optionally substituted with 1-3 substituents, each substituent independently is –C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, –CN, -C_{1-4}alkoxyl, phenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), –C_{1-4}hydroxyalkyl; or

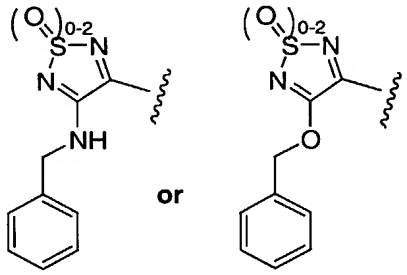
A is pyridyl, pyradazinyl, pyrimidinyl, or pyrazinyl, each optionally substituted with 1-5 substituents; each substituent independently is –C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, –CN, phenyl, pyrrolidinyl, azepanyl, –C_{1-4}hydroxyalkyl, –C_{1-4}alkoxy, $(CH_3)_2N$–$(CH_2)_2$–NH–, -SO_2-C_{1-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), –C_{0-4}alkyl–N(C_{3-6}cycloalkyl)(C_{0-5}alkyl), –C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{1-4}alkyloxyC_{1-4}alkyl), –N(C_{0-5}alkyl)–C_{0-4}alkyl-phenyl(C1-4alkoxyl)$_{0-3}$, –N(C_{0-5}alkyl)–C_{0-4}alkylthiaphenyl, dimethoxyphenyl–CH_2–NH–; any

phenyl optionally substituted with 1-5 –OH, halogen, or C_{1-4}alkyl; any alkyl optionally substituted with 1-5 –OH or halogen; or the substituent taken with a neighboring bond is =O; or

A is pyrrolophenyl, imidazolophenyl, pyrazolophenyl, triazolophenyl, pyridinoimidazolyl, naphthyridinyl, tetrahydrocyclopentopyrazolyl, quinolinyl, pyrimidinopyrazololyl, benzothiazolyl, benzoimidazolyl, benzoxazolonyl, oxodihydrobenzoxazolyl, indolinonyl, oxadihydroquinolinyl, oxatetrahydroquinolinyl, or purinyl, each optionally substituted with 1-5 substituents, each substituent independently is -C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, or –CN;

B is aryl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, heteroaryl$(CH_2)_{1-3}$–O–$(CH_2)_{0-2}$–C(O)–, indanyl$(CH_2)_{0-3}$–O–$(CH_2)_{0-2}$–C(O)–, aryl$(CH_2)_{1-3}$–C(O)–$(CH_2)_{0-2}$–, aryl–cyclopropyl–C(O)–$(CH_2)_{0-2}$–, heteroaryl$(CH_2)_{1-3}$–C(O)–, aryl$(CH_2)_{1-3}$–, heteroaryl$(CH_2)_{1-3}$–, aryl$(CH_2)_{1-3}$–NH–C(O)–, aryl$(CH_2)_{1-3}$–NH–C(NCN)–, aryl$(CH_2)_{1-3}$–SO_2–, aryl$(CH_2)_{0-3}$–S–$(CH_2)_{0-2}$–C(O)–, or heteroaryl$(CH_2)_{1-3}$–SO_2– wherein any of the aryl or heteroaryl is optionally substituted by 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, phenyl, –O–C_{1-4}alkylphenyl, –S(O)–C_{1-4}alkyl, bromo, fluoro, chloro, or 2 substituents together form methylene dioxy; any (CH_2) optionally is substituted with C_{1-2}alkyl; or

B is



wherein the phenyl is optionally substituted by 1-3 substituents, each substituent independently is C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{1-4}alkoxy, trifluoromethyl, bromo, fluoro, or chloro; and

X is H, OH, F, C_{1-4}alkyl, C_{1-4}alkoxy, –N(C_{0-5}alkyl)(C_{0-5}alkyl), phenyl, or =O.

2. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein

NonAr is a nonaromatic 6 membered ring containing 1 nitrogen ring atom, wherein the remaining ring atoms are carbon.

3. The compound according to Claim 2, or a pharmaceutically acceptable salt thereof, wherein

A is a phenyl optionally substituted with 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-7}cycloalkyl, -CF_3, halogen, -OH, –CN, imidazolyl, -C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), -O-C_{1-4}alkyl, -C(O)-C_{0-4}alkyl, -C(O)-O-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkylphenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O-C_{1-4}alkyl, or –$NHSO_2$-C_{1-4}alkyl, -O-C_{1-4}alkylphenyl, or hydroxyiminoethyl; any alkyl optionally substituted with 1-6 –OH or halogen.

4. The compound according to Claim 2, or a pharmaceutically acceptable salt thereof, wherein

A is pyrrolyl, imidazolyl, pyrazolyl, triazolyl, thiophenyl, thiazolyl, thiadiazolyl, oxazolyl, or isoxazolyl, each optionally substituted with 1-3 substituents, each substituent independently is –C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, –CN, phenyl, –C_{1-4}hydroxyalkyl.

5. The compound according to Claim 2, or a pharmaceutically acceptable salt thereof, wherein

A is pyridyl, pyradazinyl, pyrimidinyl, or pyrazinyl, each optionally substituted with 1-3 substituents, each substituent independently is –C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, –CN, phenyl, –C_{1-4}hydroxyalkyl, –C_{1-4}alkoxy, $(CH_3)_2N$–$(CH_2)_2$–NH–, –C_{0-4}alkyl–N(C_{0-4}alkyl)(C_{0-4}alkyl), dimethoxyphenyl–CH_2–NH–, or the substituent taken with a neighboring bond is =O.

6. The compound according to Claim 2, or a pharmaceutically acceptable salt thereof, wherein

A is pyrrolophenyl, imidazolophenyl, pyrazolophenyl, triazolophenyl, pyridinoimidazolyl, naphthyridinyl, tetrahydrocyclopentopyrazolyl, quinolinyl, pyrimidinopyrazololyl, benzothiazolyl, benzoimidazolyl, or purinyl, each optionally

substituted with 1-3 substituents, each substituent independently is –C_{1-4}alkyl, –C_{3-7}cycloalkyl, –CF_3, halogen, –OH, or –CN.

7. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein

NonAr is a nonaromatic 5 membered ring containing 1 nitrogen ring atom, wherein the remaining ring atoms are carbon.

8. The compound according to Claim 7, or pharmaceutically acceptable salts thereof, wherein

A is a phenyl optionally substituted with 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-7}cycloalkyl, -CF_3, halogen, -OH, –CN, imidazolyl, -C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), -O-C_{1-4}alkyl, -C(O)-C_{0-4}alkyl, -C(O)-O-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkylphenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O-C_{1-4}alkyl, or –$NHSO_2$-C_{1-4}alkyl, -O-C_{1-4}alkylphenyl, or hydroxyiminoethyl; any alkyl optionally substituted with 1-6 –OH or halogen.

9. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein

NonAr is a nonaromatic 6 membered ring containing 2 nitrogen ring atoms, wherein the remaining ring atoms are carbon.

10. The compound according to Claim 9, or pharmaceutically acceptable salts thereof, wherein

A is a phenyl optionally substituted with 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-7}cycloalkyl, -CF_3, halogen, -OH, –CN, imidazolyl, -C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), -O-C_{1-4}alkyl, -C(O)-C_{0-4}alkyl, -C(O)-O-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkylphenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O-C_{1-4}alkyl, or –$NHSO_2$-C_{1-4}alkyl, -O-C_{1-4}alkylphenyl, or hydroxyiminoethyl; any alkyl optionally substituted with 1-6 –OH or halogen.

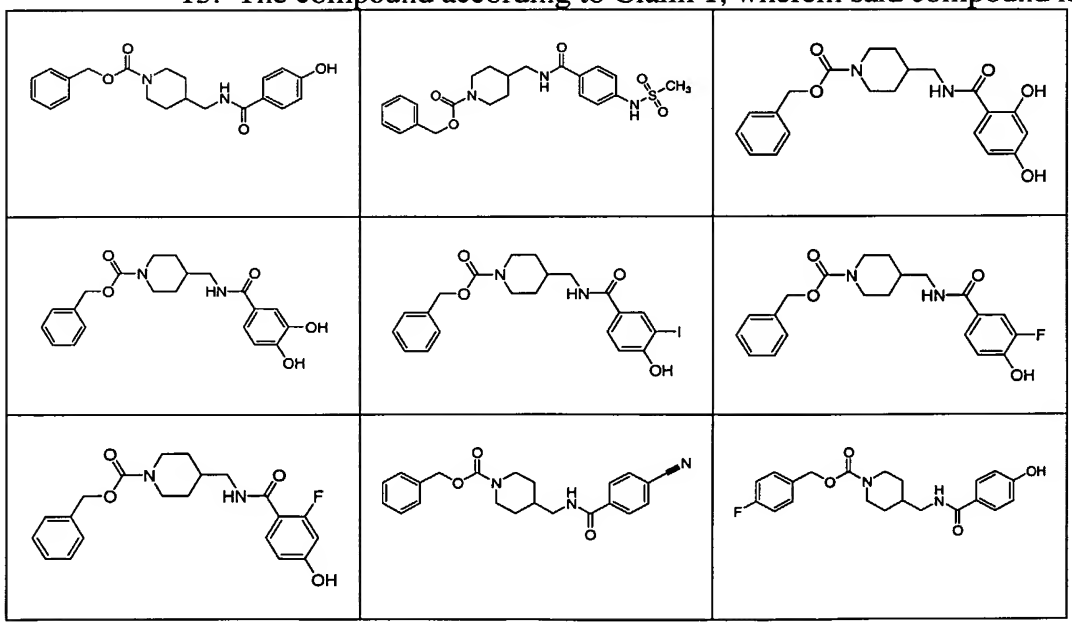
11. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein

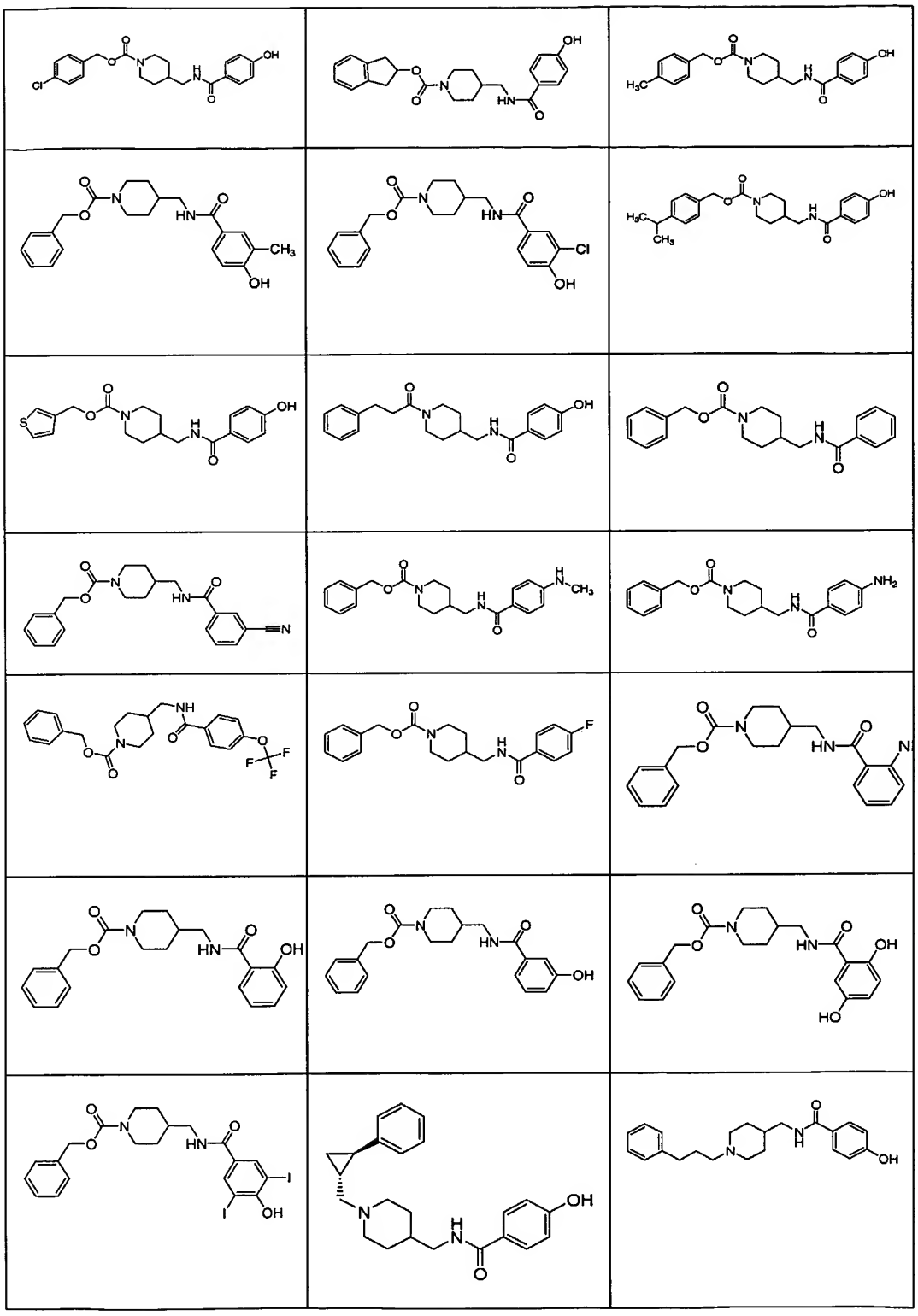
NonAr is a nonaromatic 6 membered ring containing 1 nitrogen and 1 oxygen ring atom, wherein the remaining ring atoms are carbon.

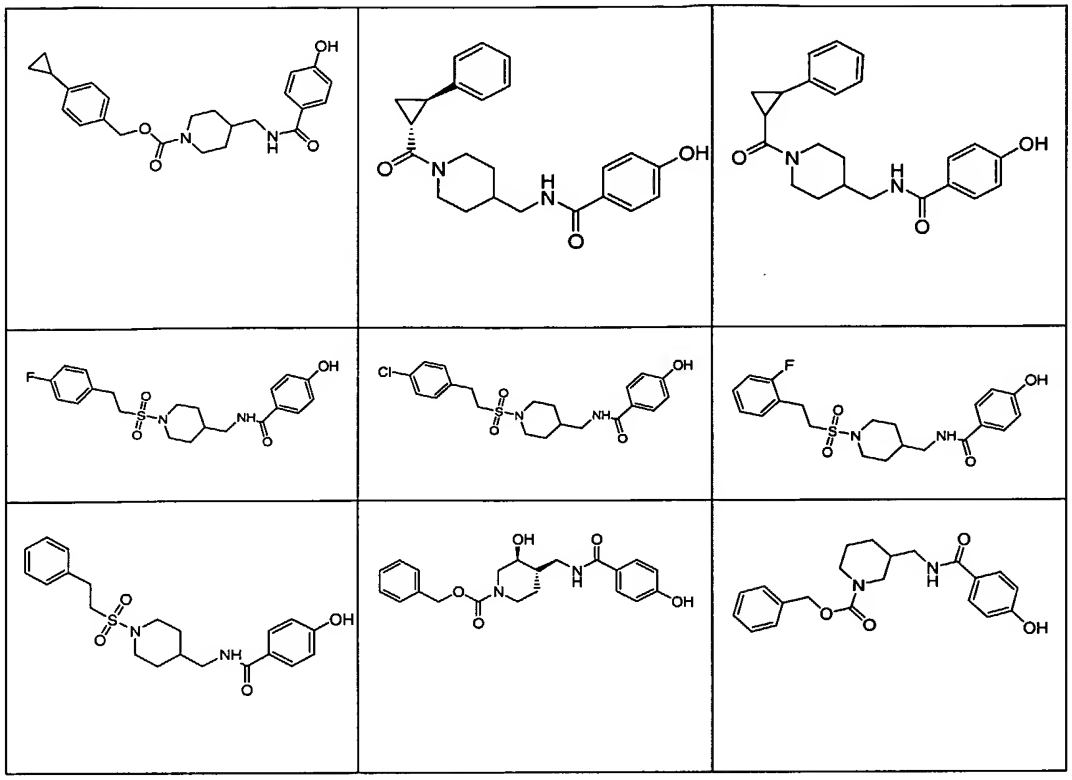
12. The compound according to Claim 11, or a pharmaceutically acceptable salt thereof, wherein

A is a phenyl optionally substituted with 1-5 substituents, each substituent independently is C_{1-4}alkyl, C_{3-7}cycloalkyl, -CF_3, halogen, -OH, –CN, imidazolyl, -C_{0-4}alkyl–N(C_{0-5}alkyl)(C_{0-5}alkyl), -O-C_{1-4}alkyl, -C(O)-C_{0-4}alkyl, -C(O)-O-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkyl, -O-C(O)-C_{0-4}alkylphenyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O–C_{0-4}alkyl, –C_{0-4}alkyl–N(C_{0-5}alkyl)–C(O)–O-C_{1-4}alkyl, or –$NHSO_2$-C_{1-4}alkyl, -O-C_{1-4}alkylphenyl, or hydroxyiminoethyl; any alkyl optionally substituted with 1-6 –OH or halogen.

13. The compound according to Claim 1, wherein said compound is

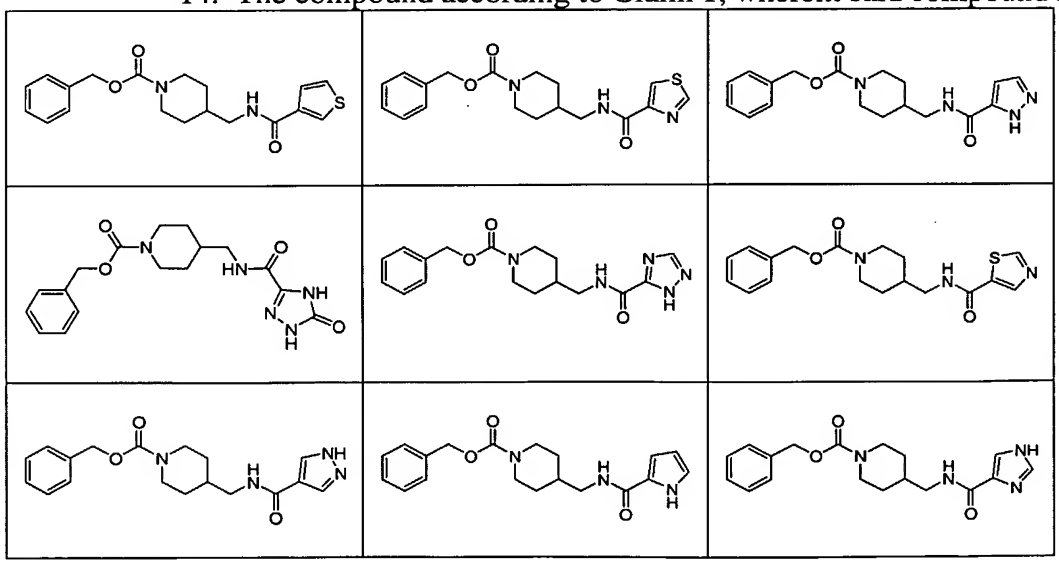


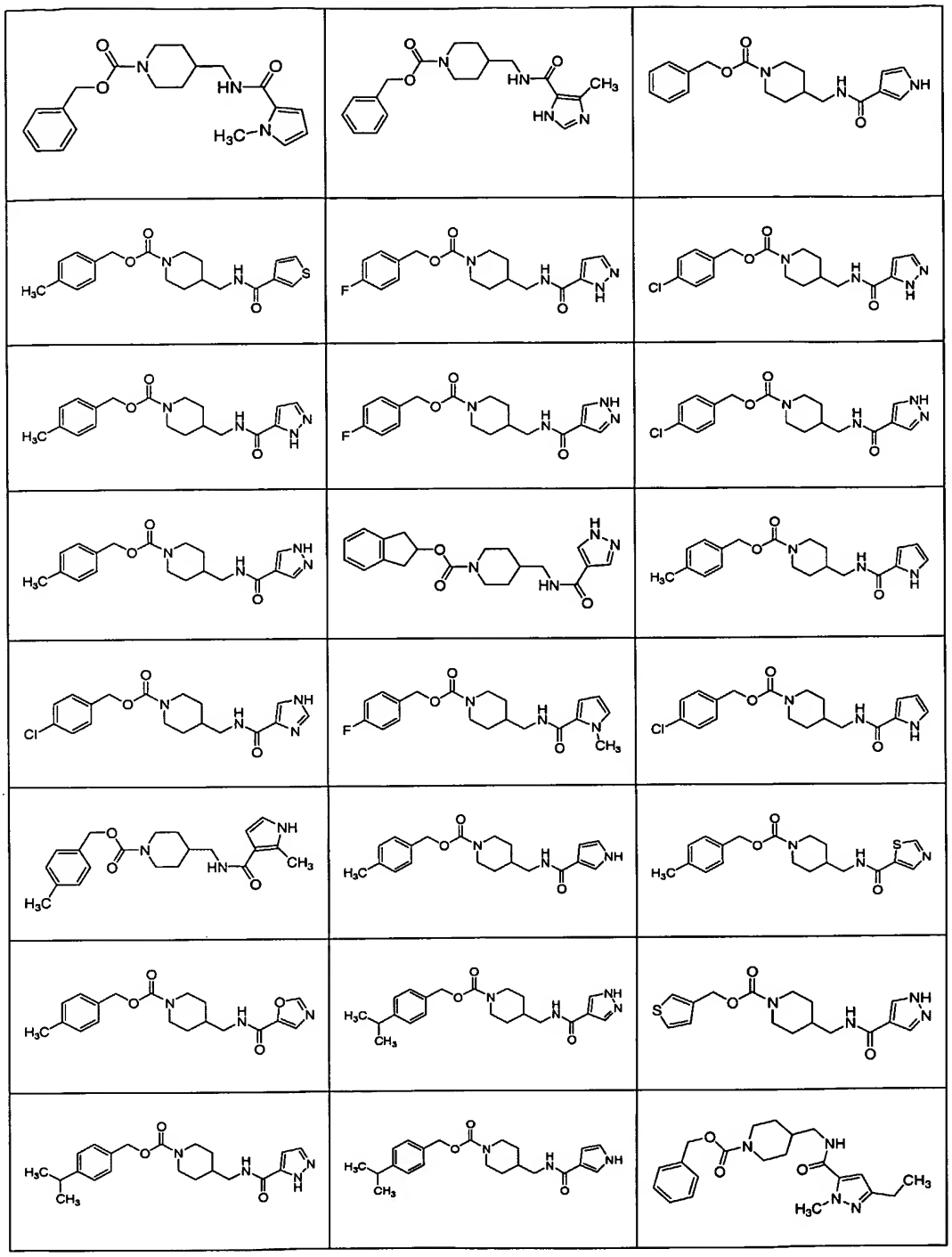


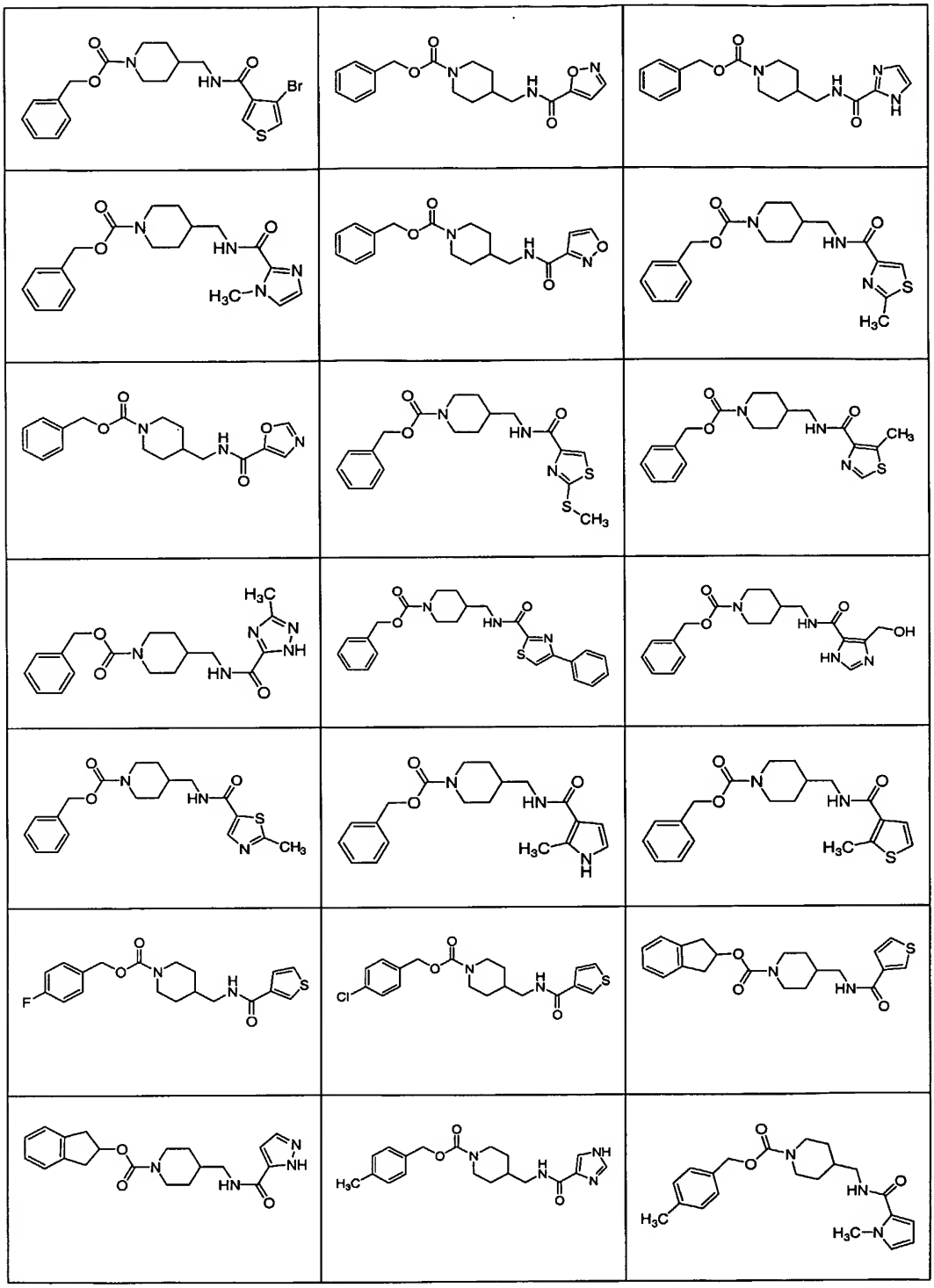


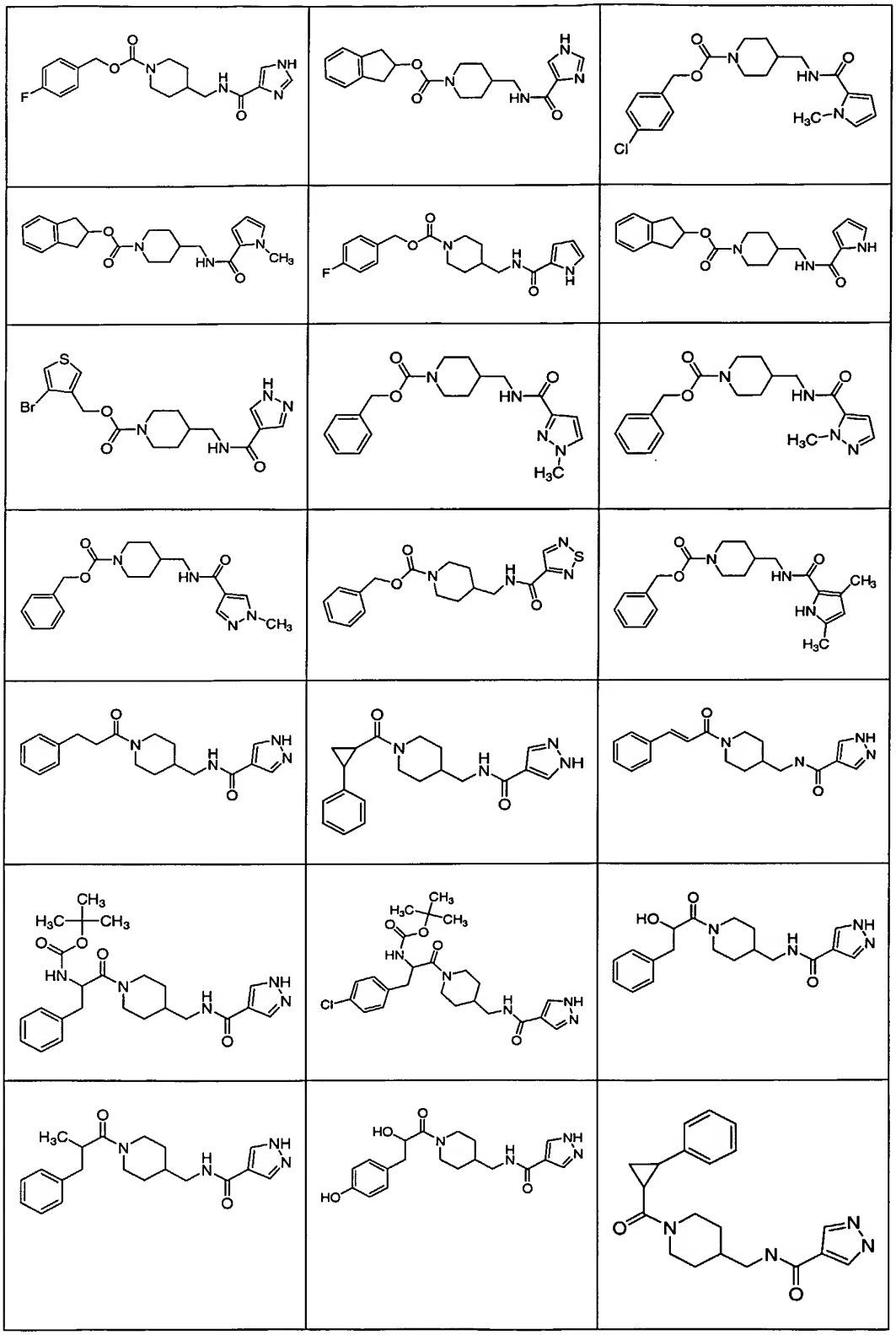
or a pharmaceutically acceptable salt thereof.

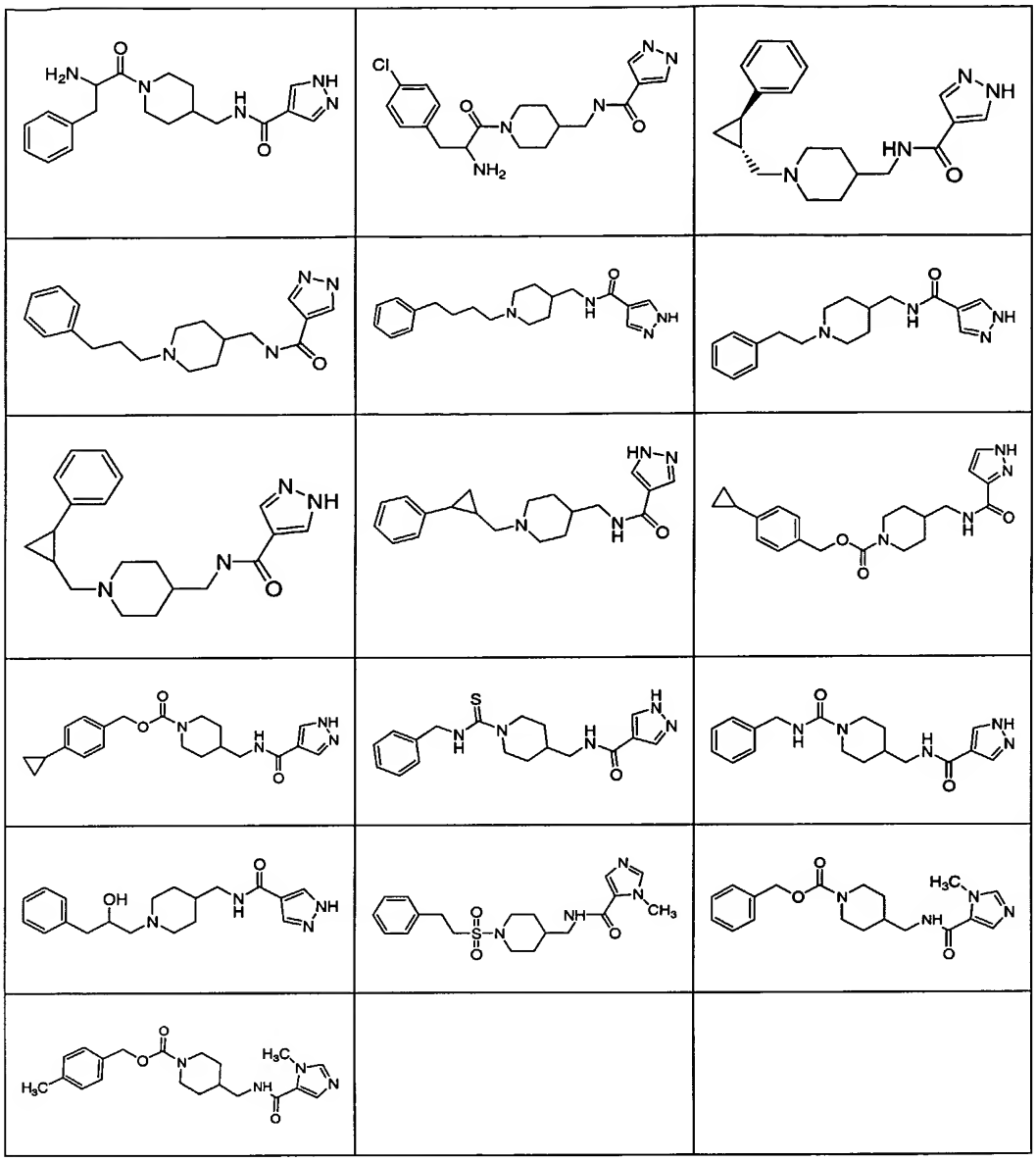
14. The compound according to Claim 1, wherein said compound is





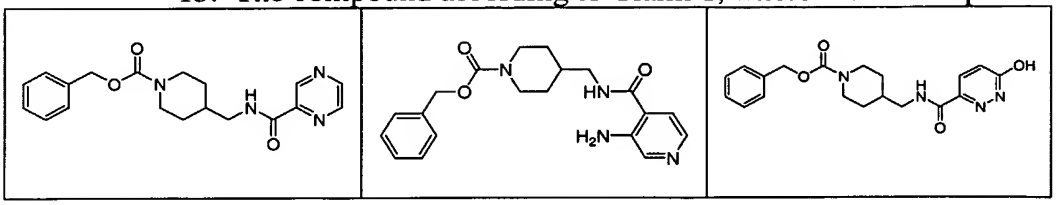


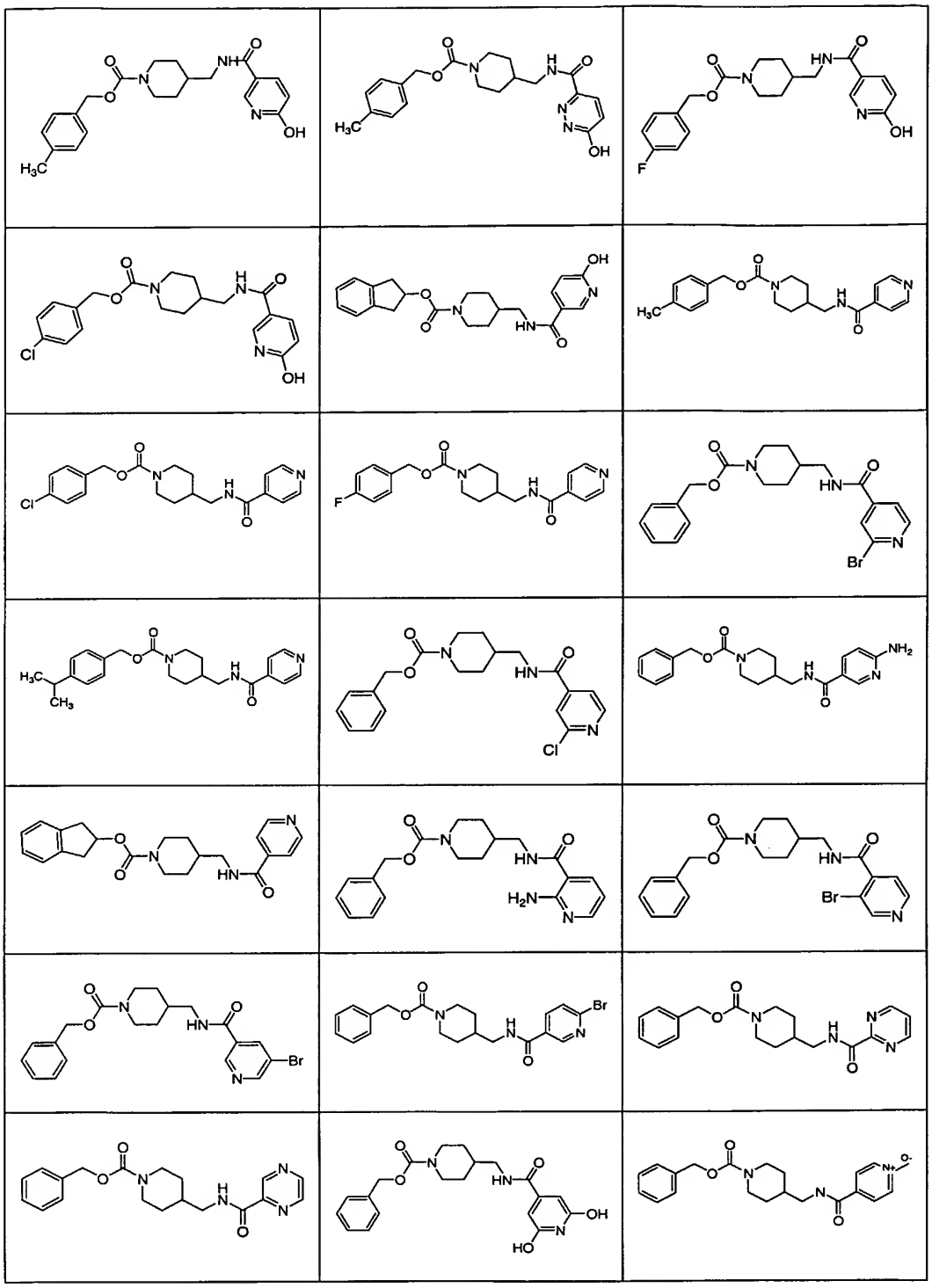


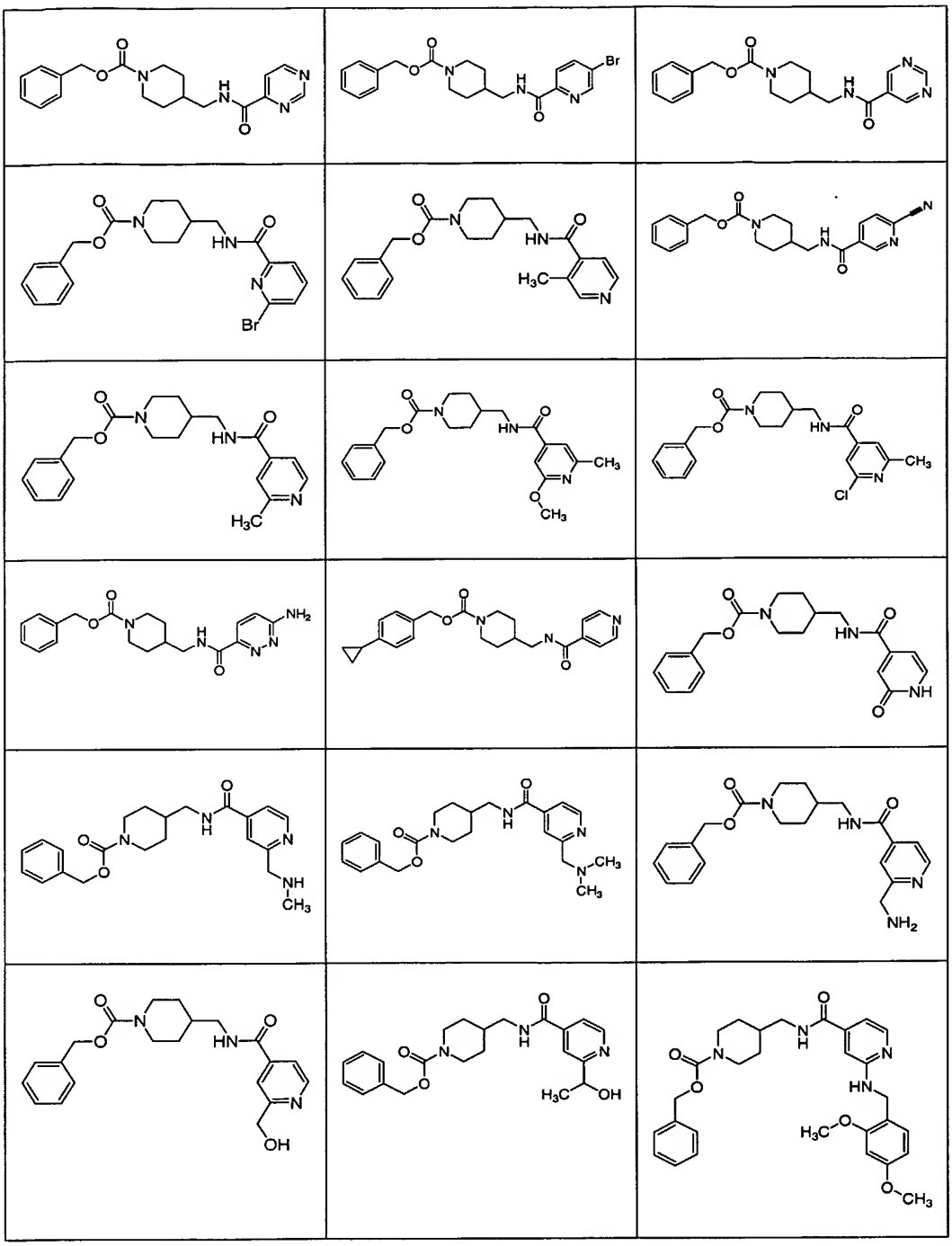


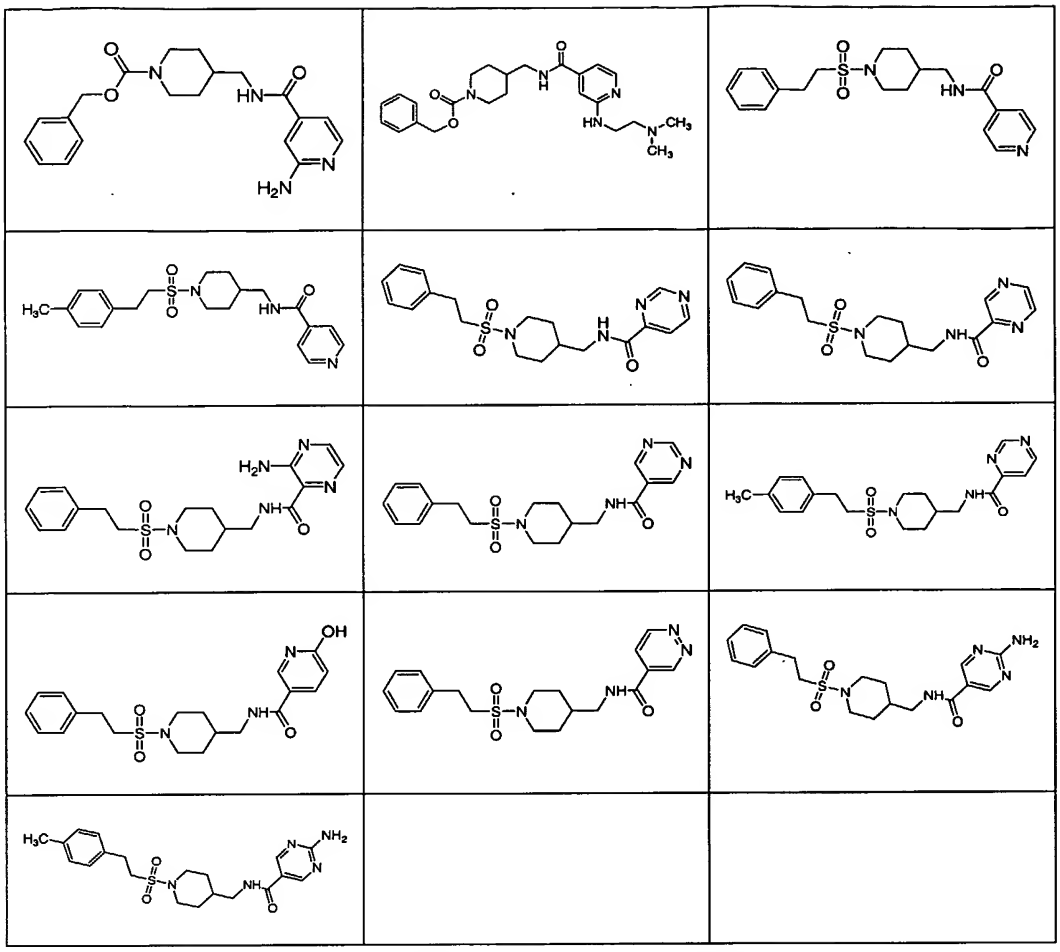
or a pharmaceutically acceptable salt thereof.

15. The compound according to Claim 1, wherein said compound is



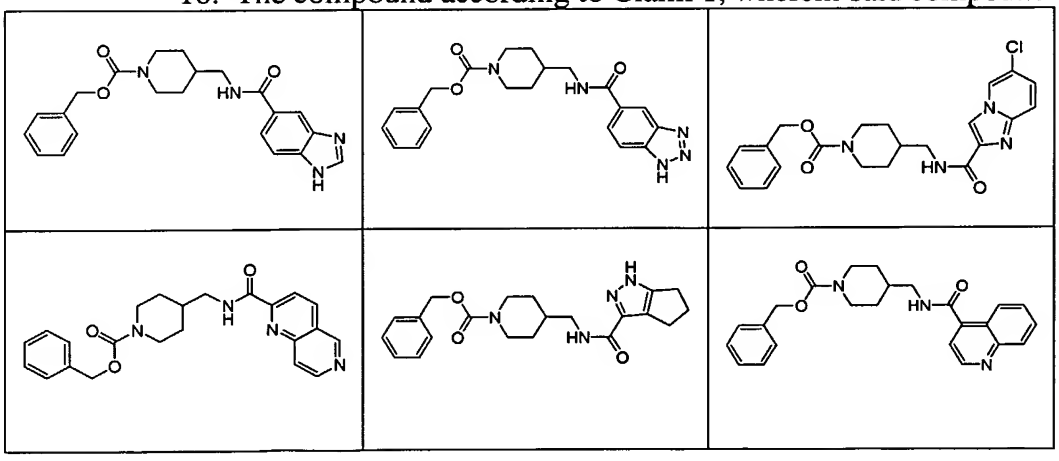


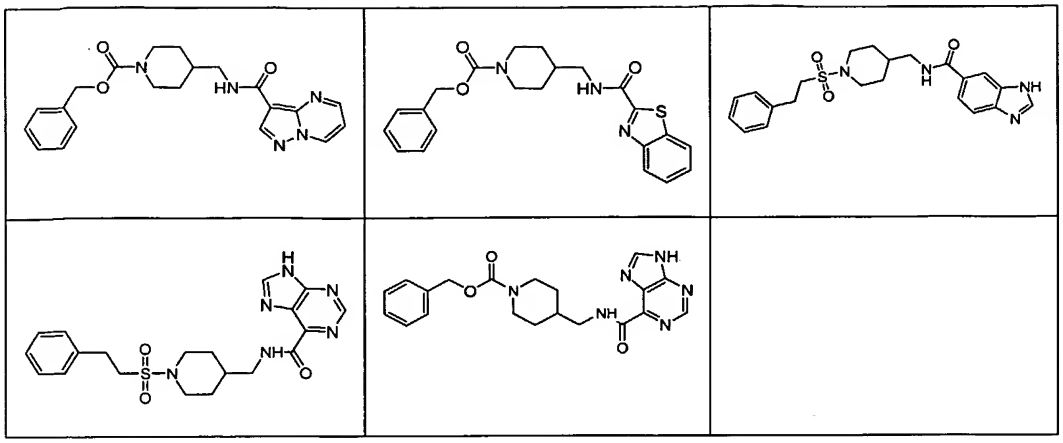




or a pharmaceutically acceptable salt thereof.

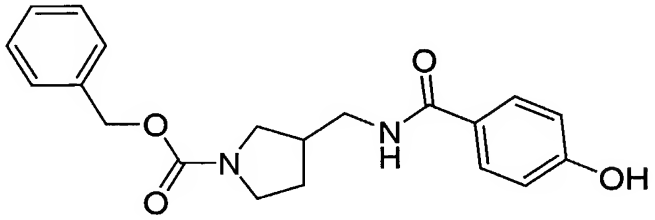
16. The compound according to Claim 1, wherein said compound is





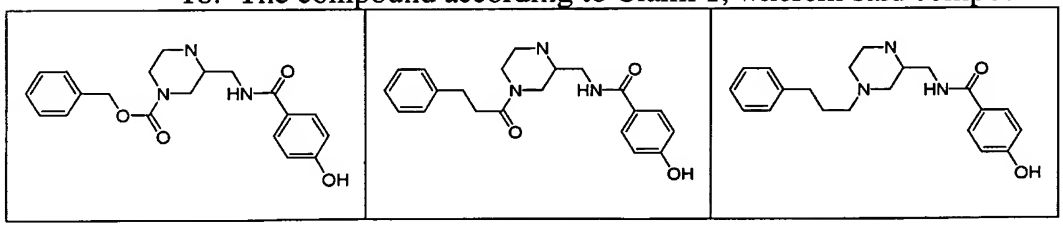
or a pharmaceutically acceptable salt thereof.

17. The compound according to Claim 1, wherein said compound is



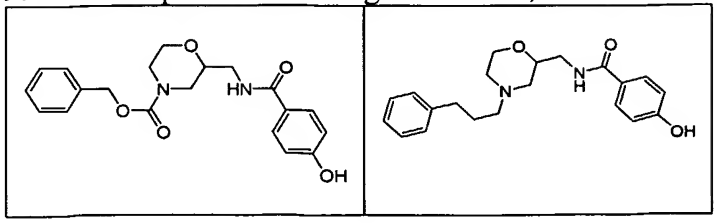
or a pharmaceutically acceptable salt thereof.

18. The compound according to Claim 1, wherein said compound is



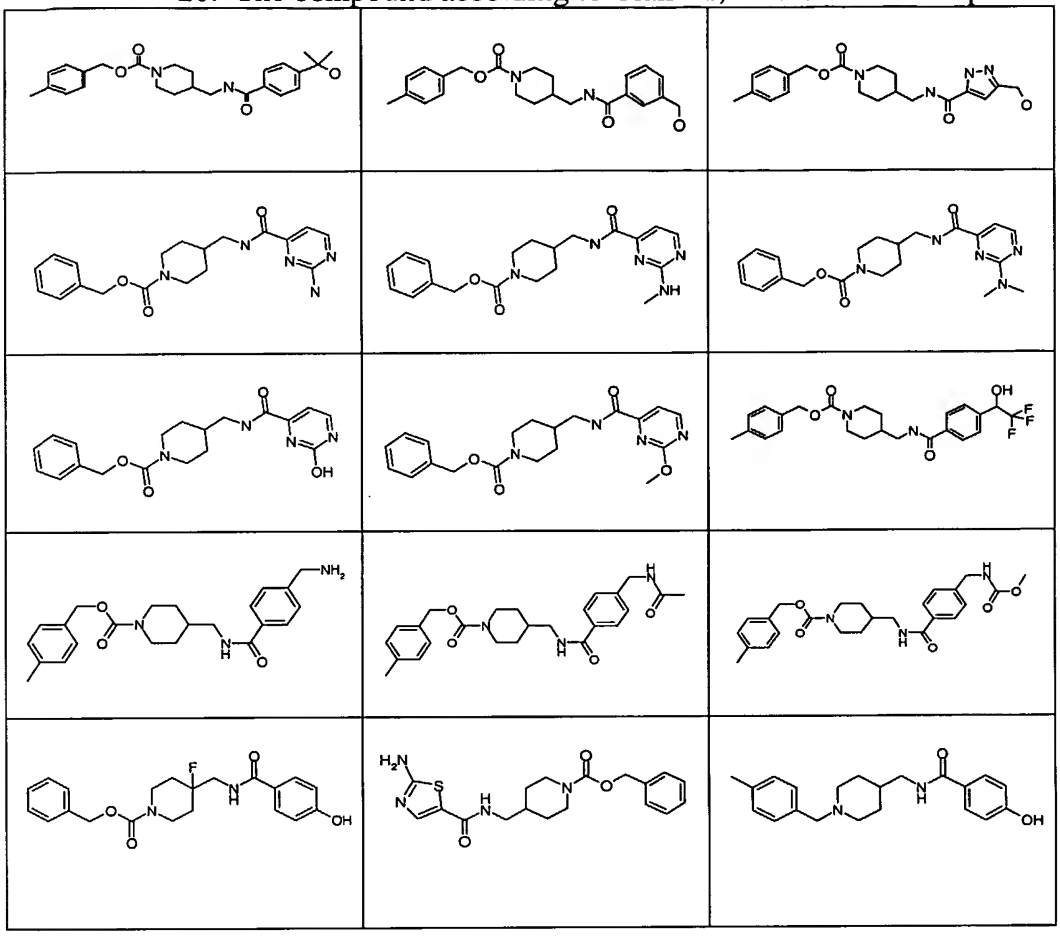
or a pharmaceutically acceptable salt thereof.

19. The compound according to Claim 1, wherein said compound is



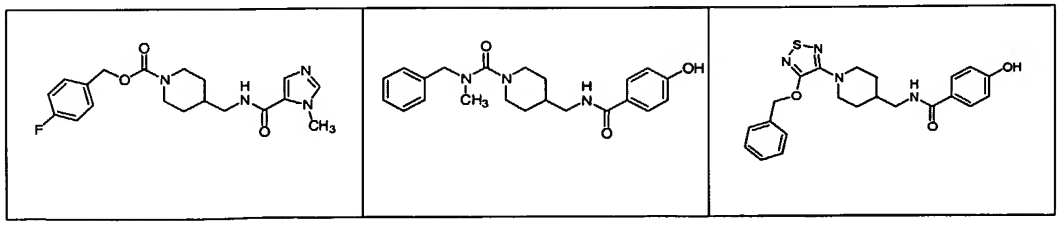
or a pharmaceutically acceptable salt thereof.

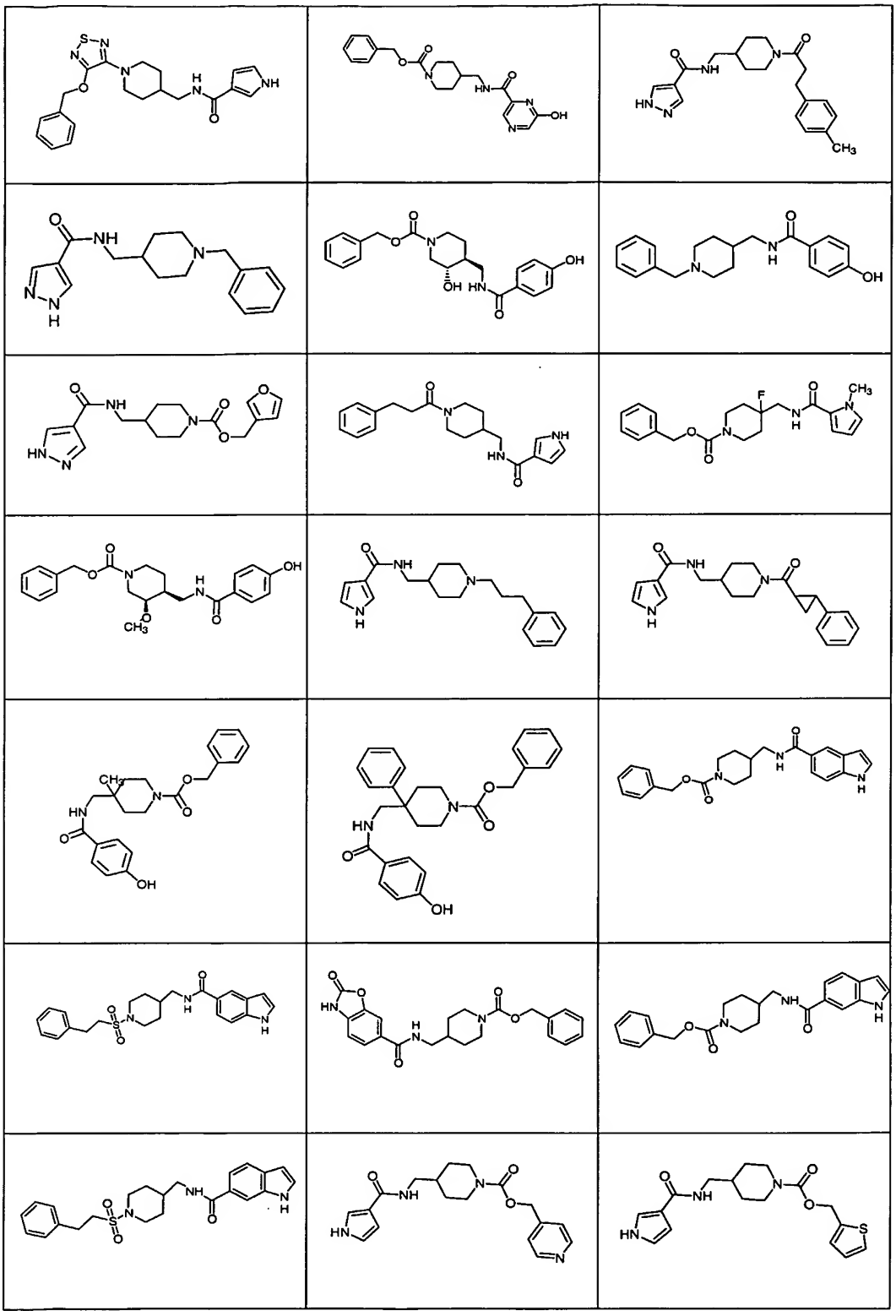
20. The compound according to Claim 1, wherein said compound is

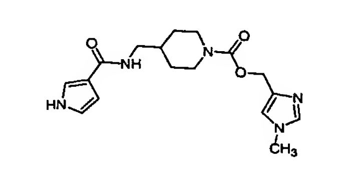
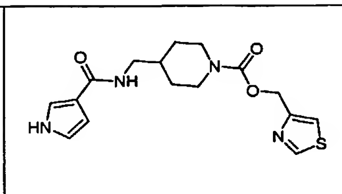
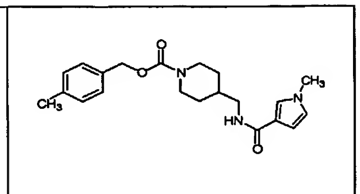
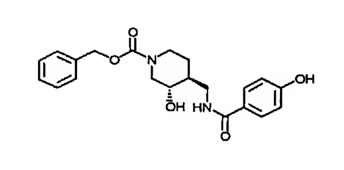
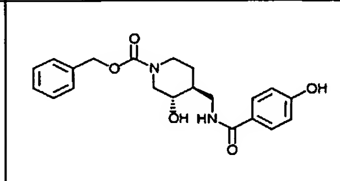
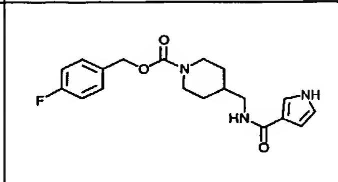
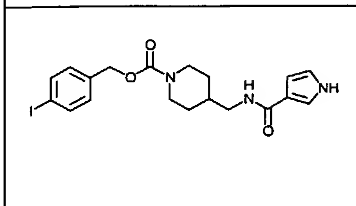
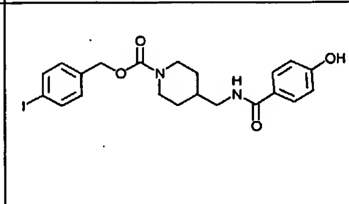
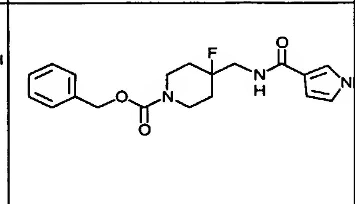
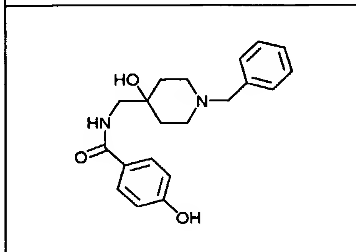
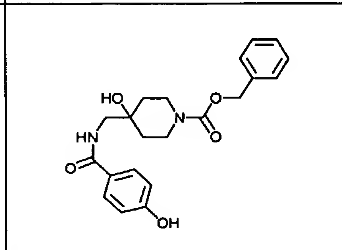
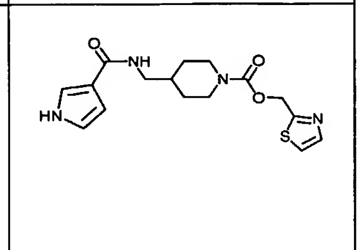
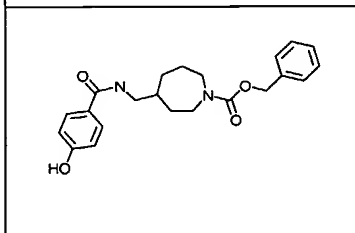
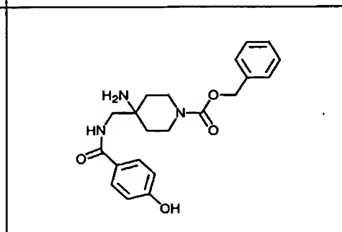
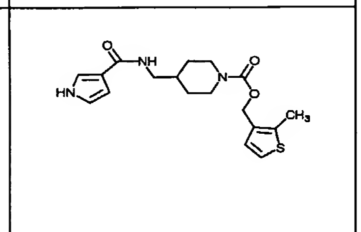
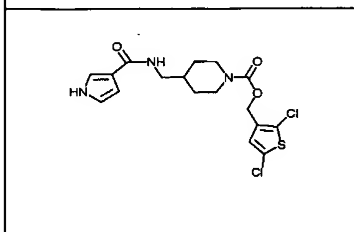
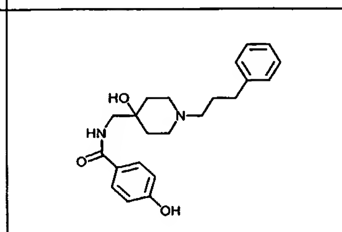
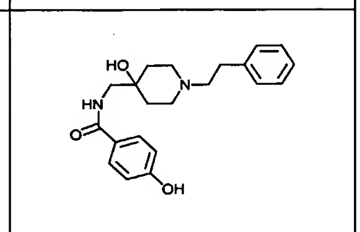
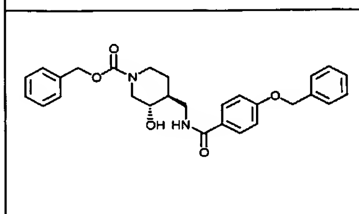
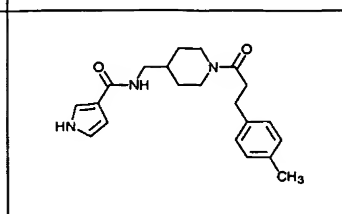
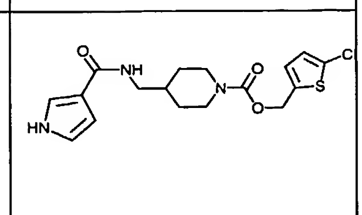


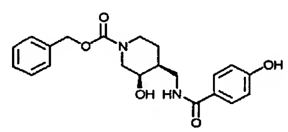
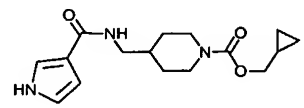
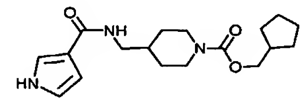
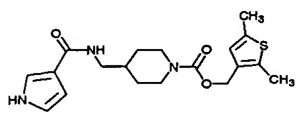
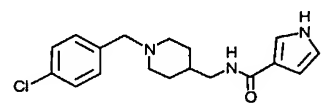
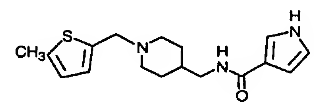
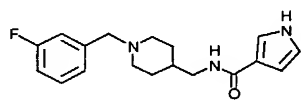
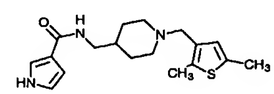
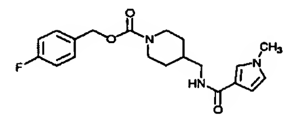
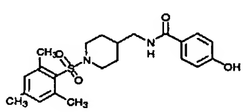
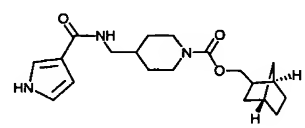
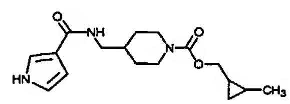
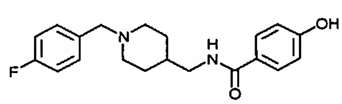
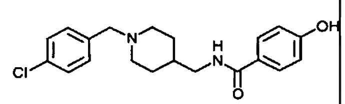
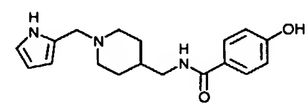
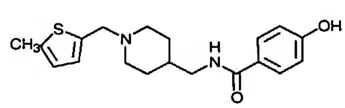
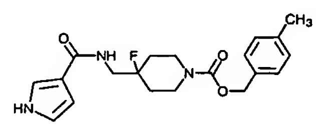
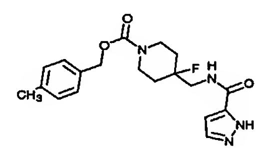
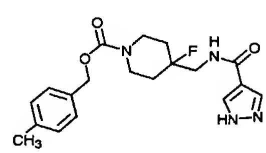
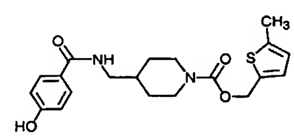
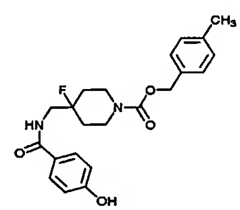
or a pharmaceutically acceptable salt thereof.

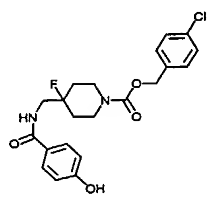
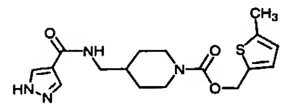
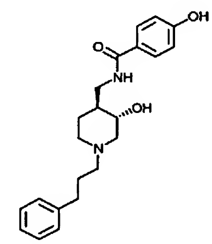
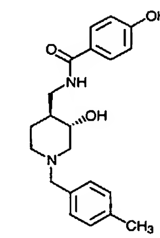
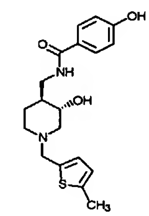
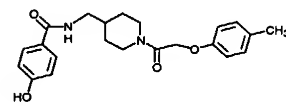
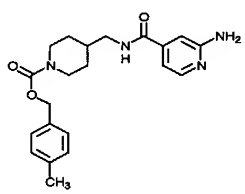
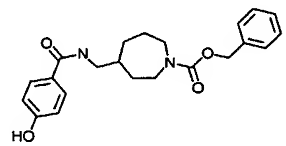
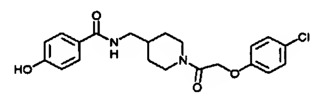
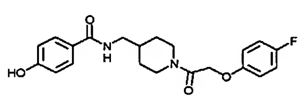
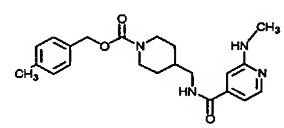
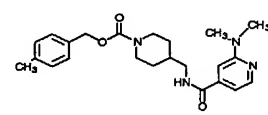
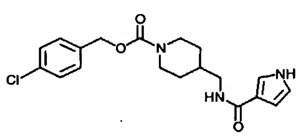
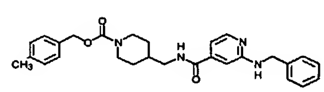
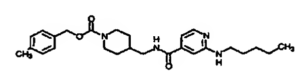
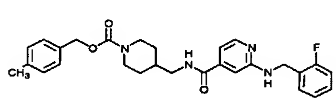
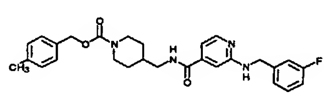
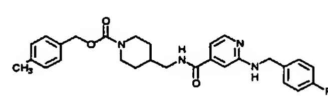
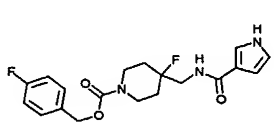
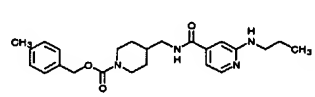
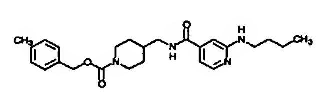
21. The compound according to Claim 1, wherein said compound is

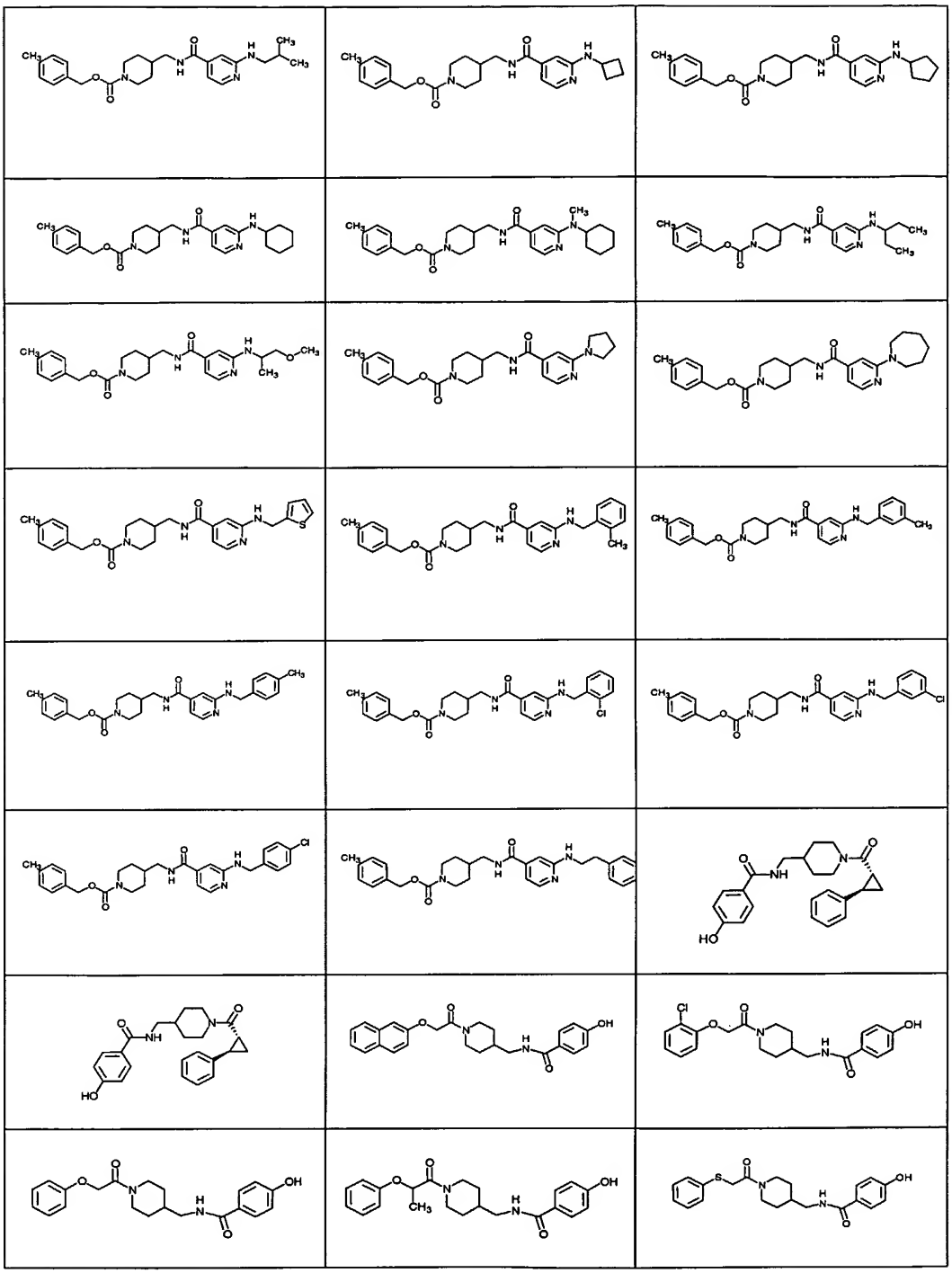


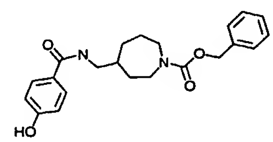
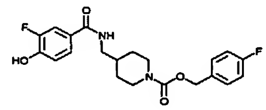
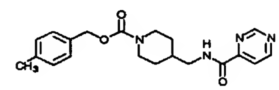
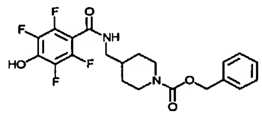
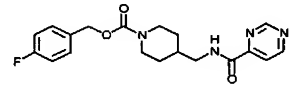
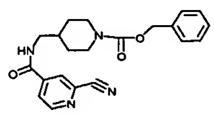
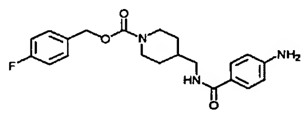
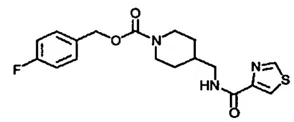
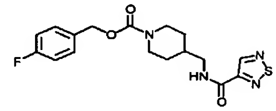
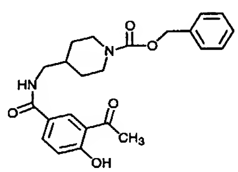
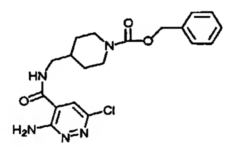
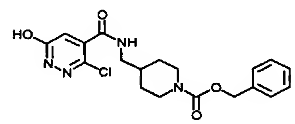
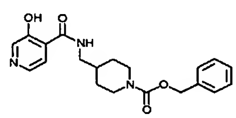
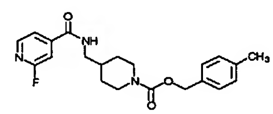
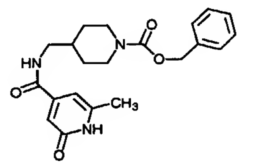
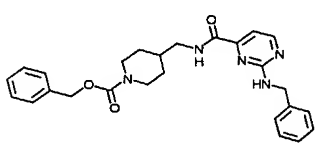
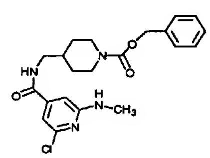
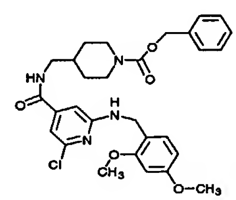
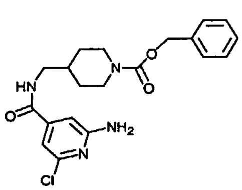
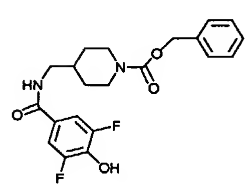
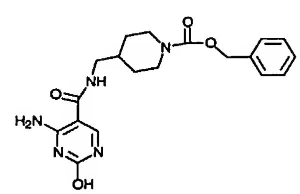


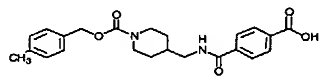
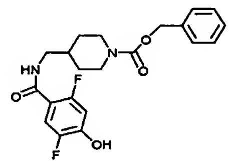
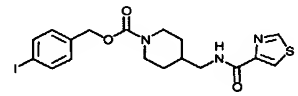
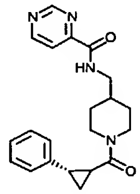
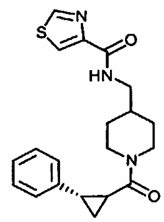
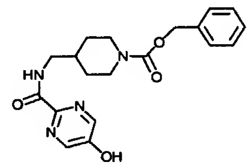
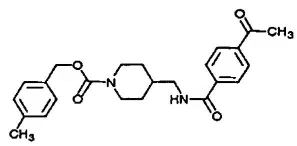
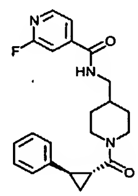
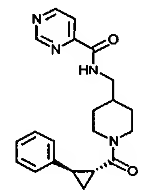
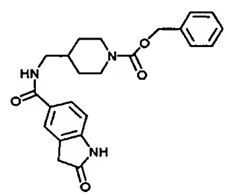
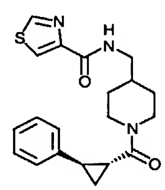
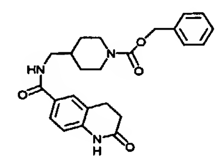
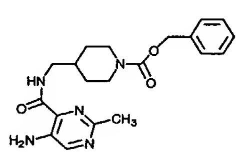
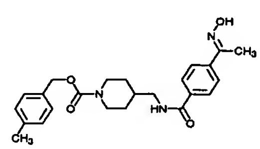
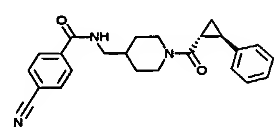
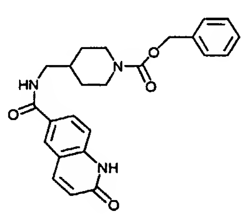
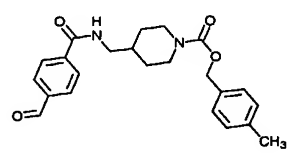
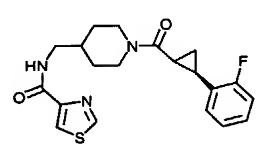
		
		
		
		
		
		
		

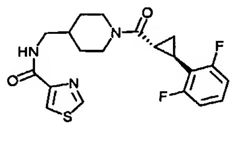
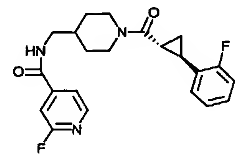
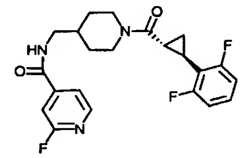
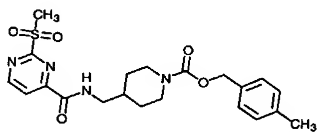
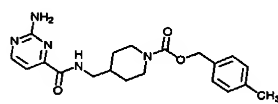
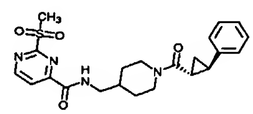
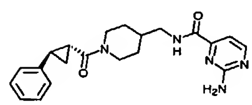
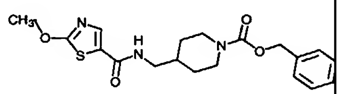
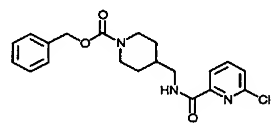
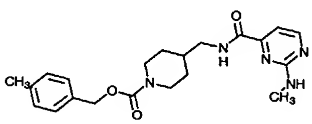
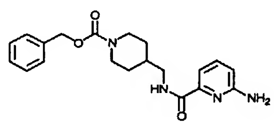
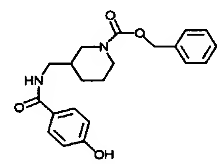
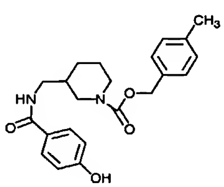
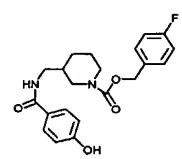
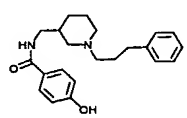
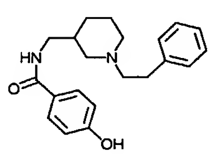
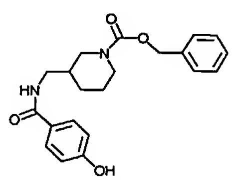
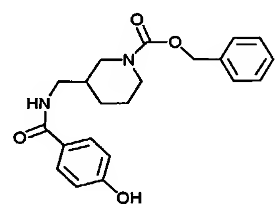
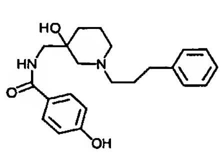
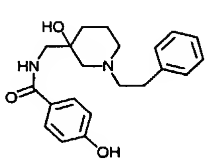
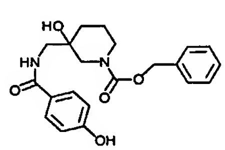
		
		
		
		
		
		
		

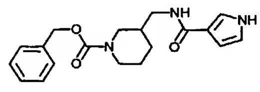
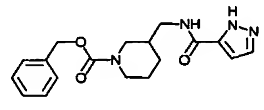
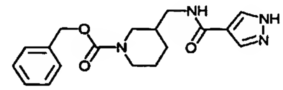
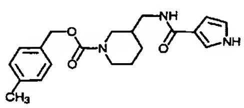
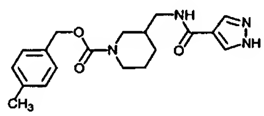
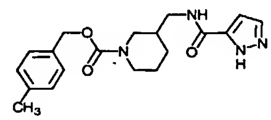
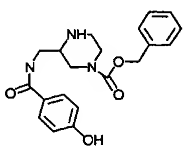
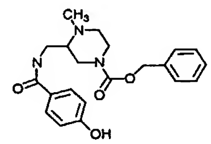
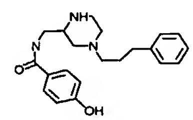
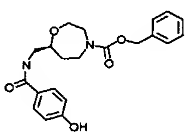
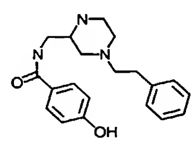
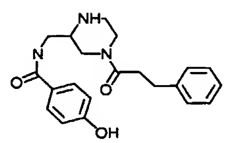
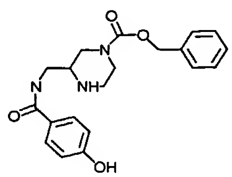
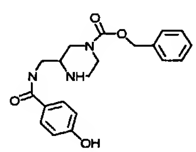
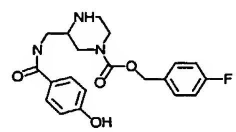
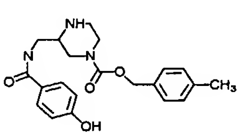
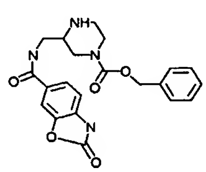
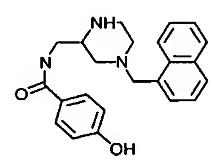
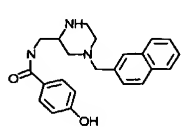
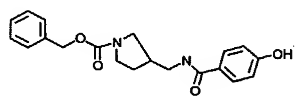
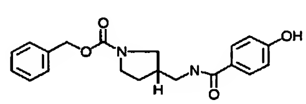
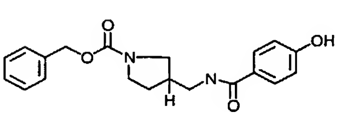
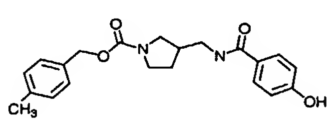
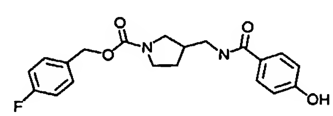
		
		
		
		
		
		
		

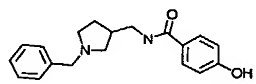
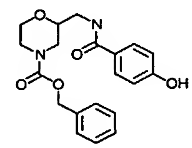
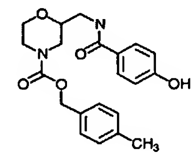
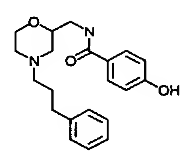
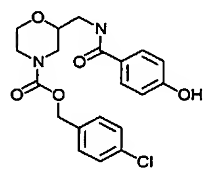
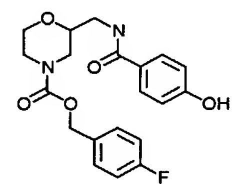
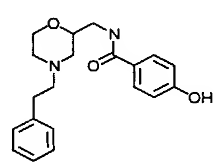
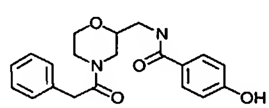
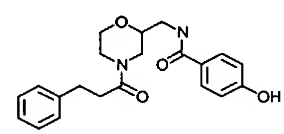
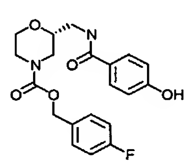
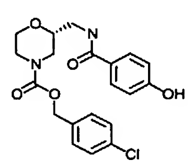
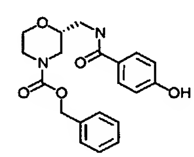
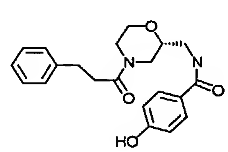
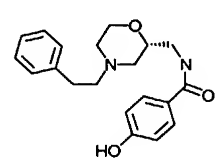
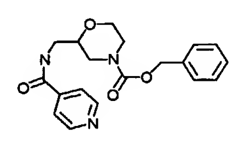
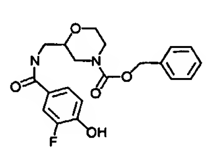
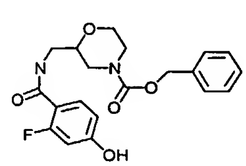
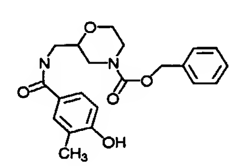
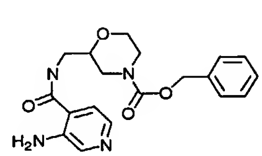
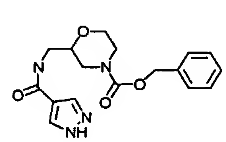
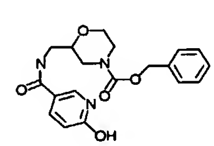


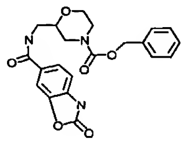
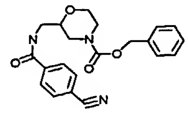
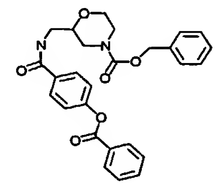
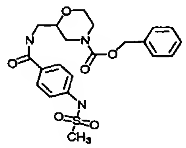
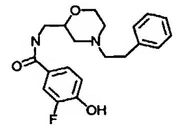
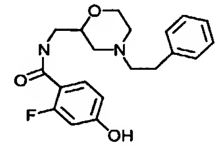
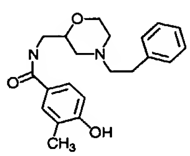
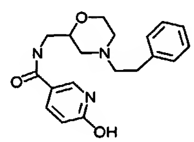
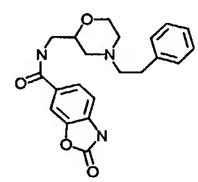
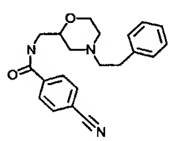
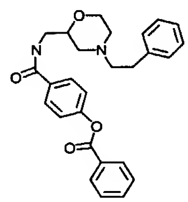
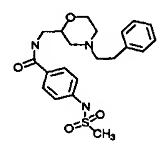
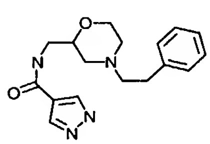
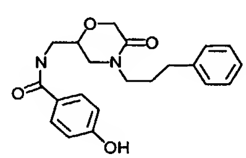
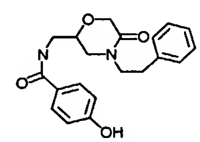
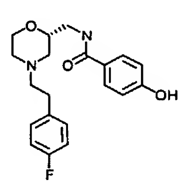
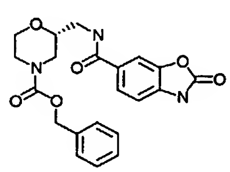
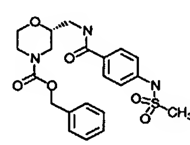
		
		
		
		
		
		
		

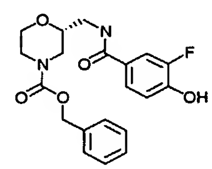
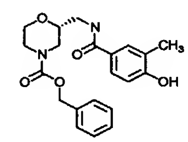
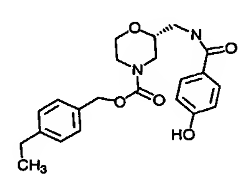
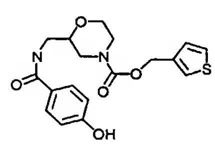
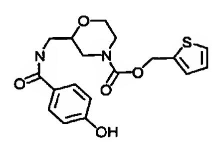
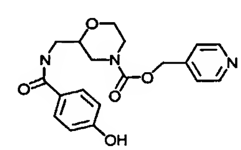
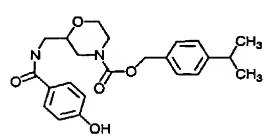
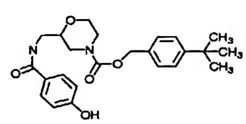
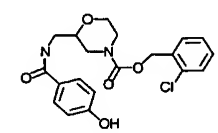
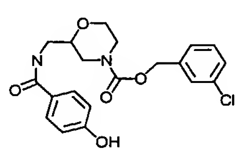
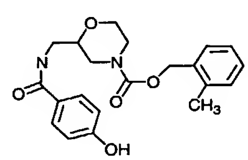
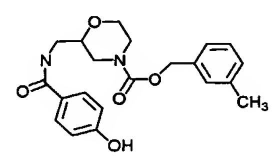
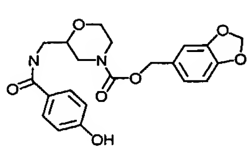
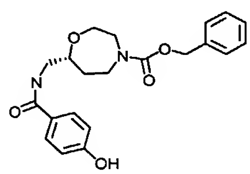
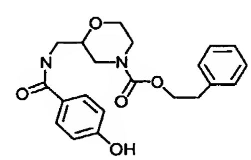
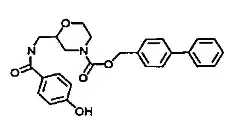
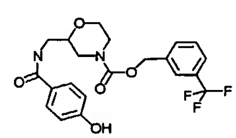
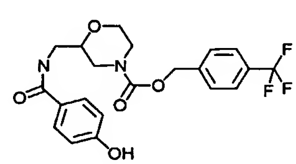
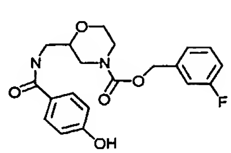
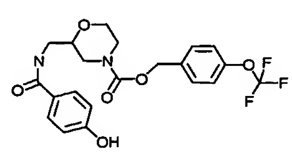
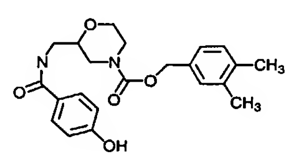
		
		
		
		
		
		

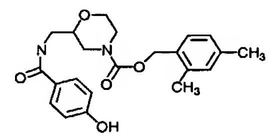
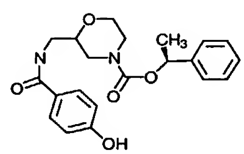
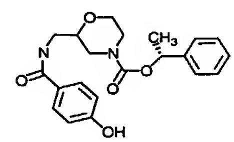
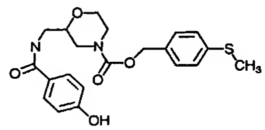
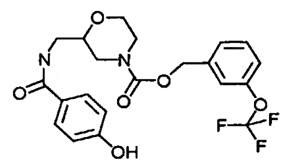
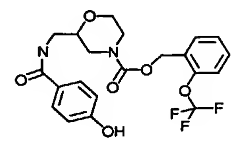
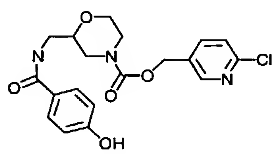
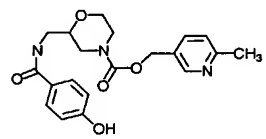
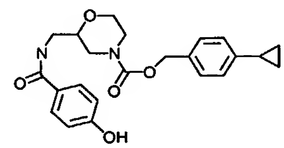
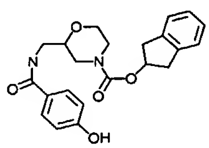
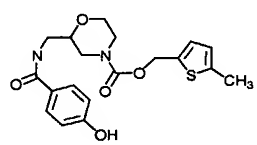
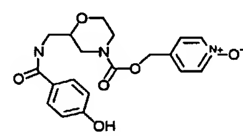
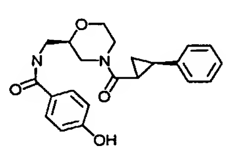
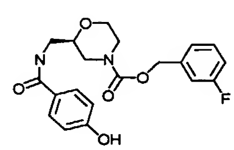
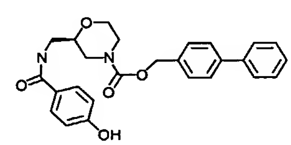
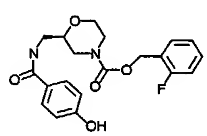
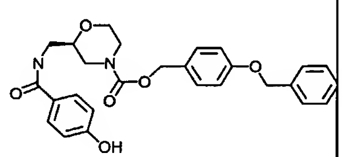
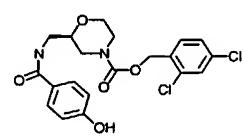
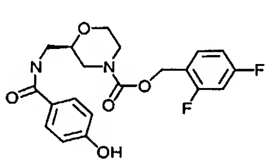
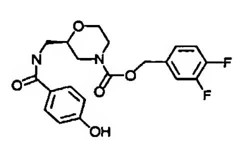
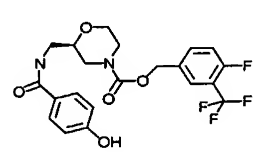
		
		
		
		
		
		
		

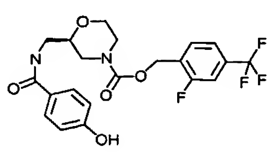
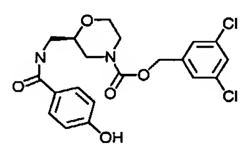
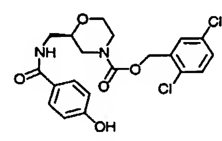
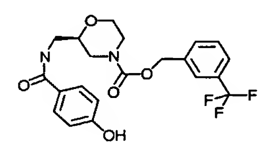
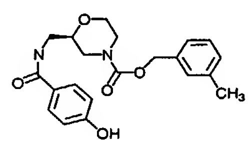
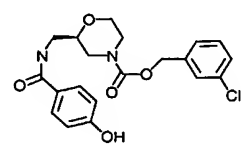
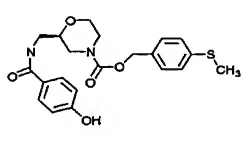
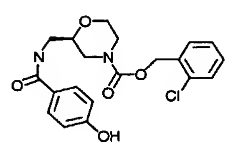
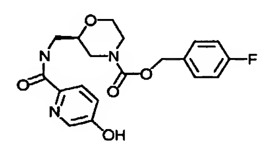
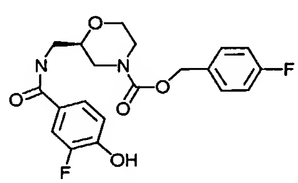
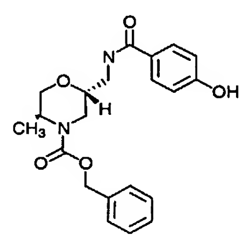
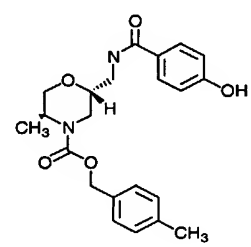
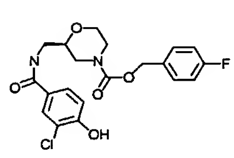
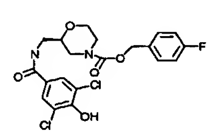
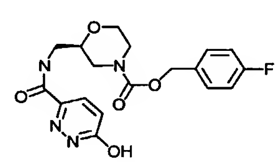
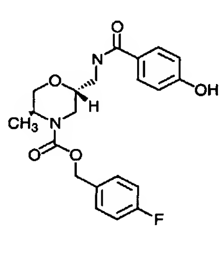
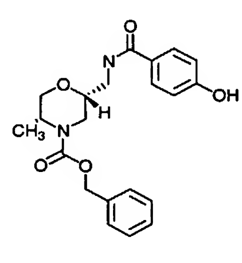
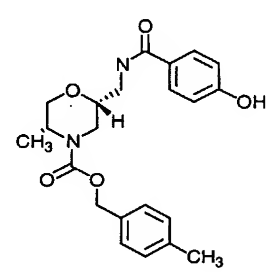
		
		
		
		
		
		
		
		

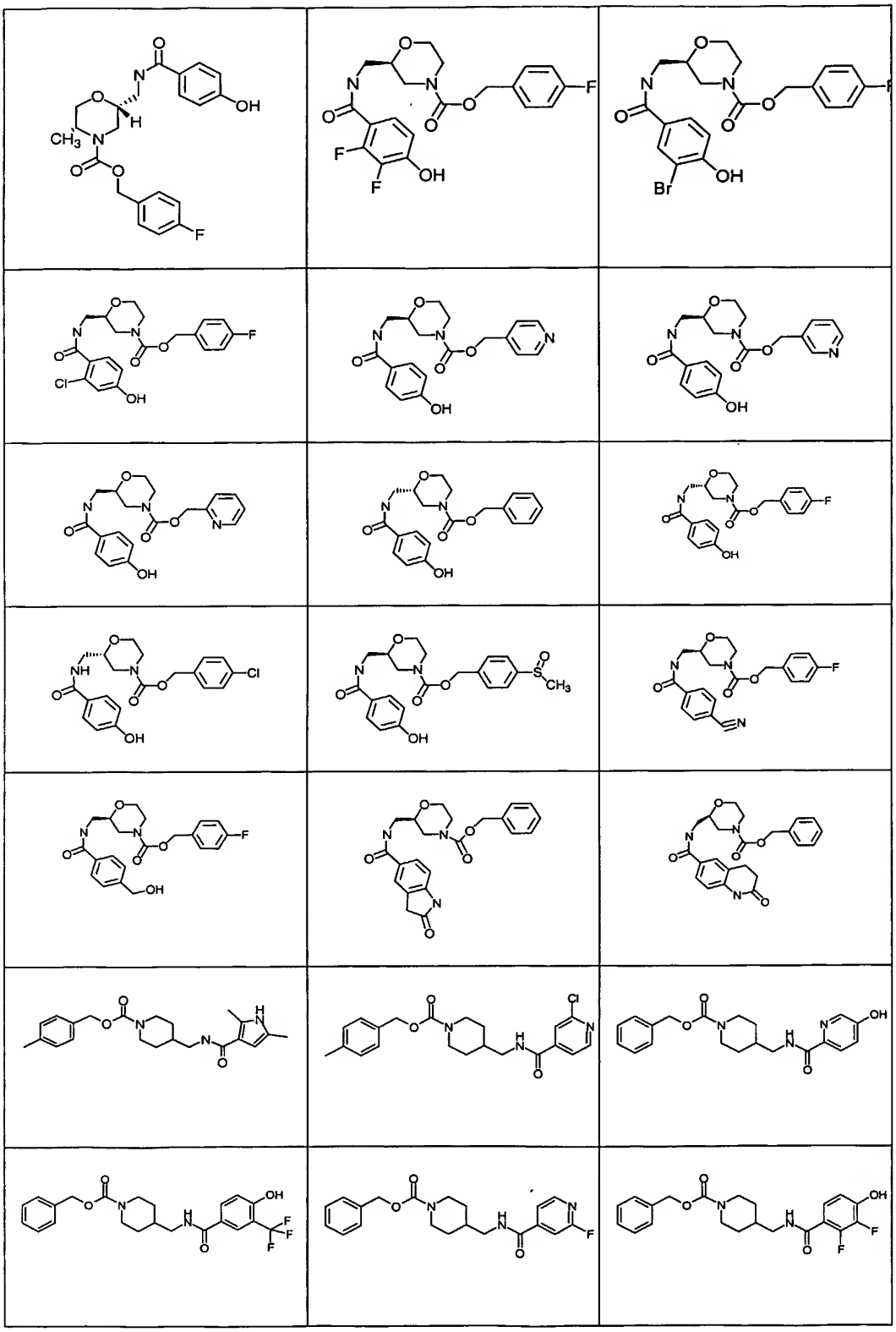
		
		
		
		
		
		
		

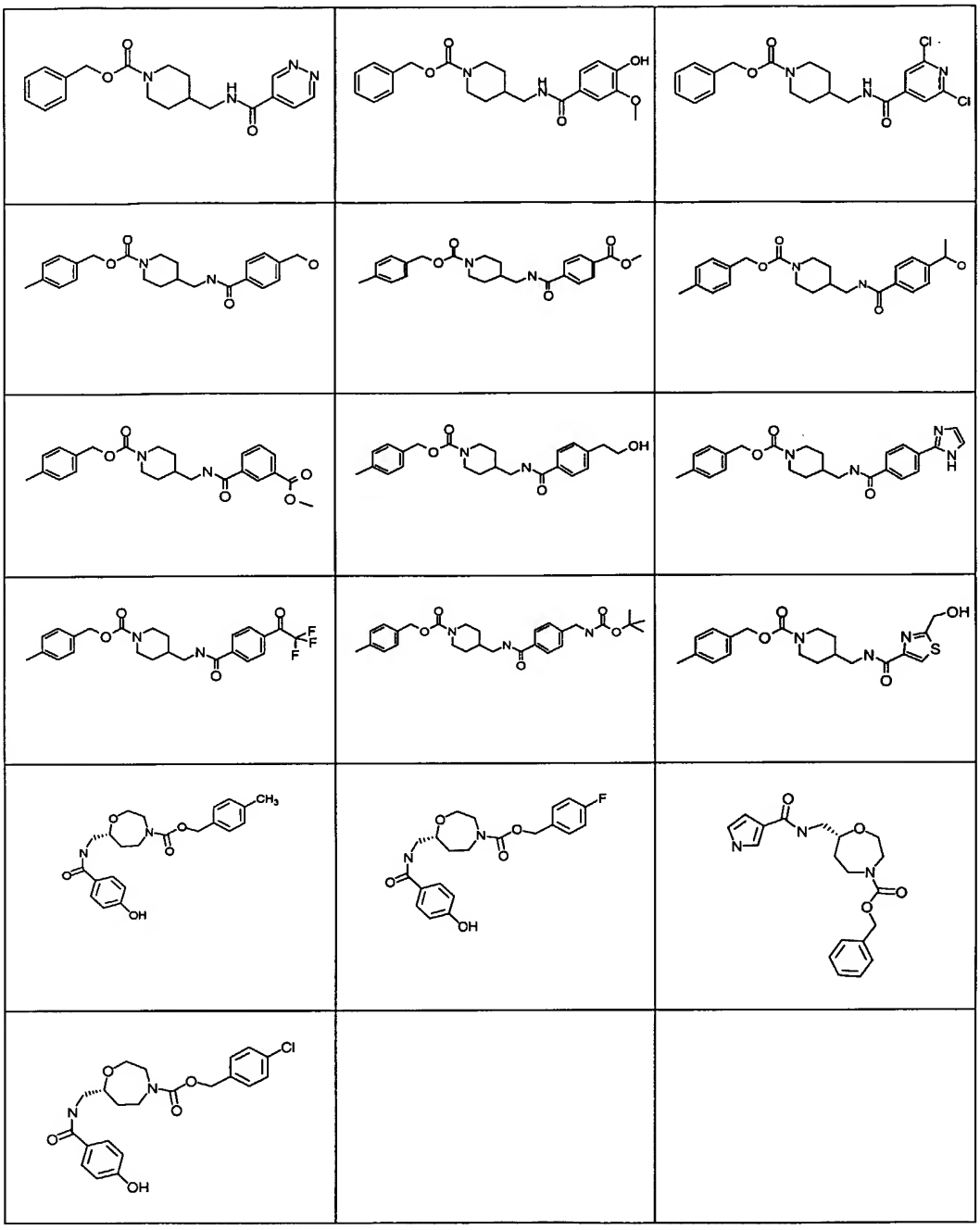
		
		
		
		
		
		





or a pharmaceutically acceptable salt thereof.

22. A pharmaceutical composition comprising an inert carrier and an effective amount of a compound according to claim 1.

23. The pharmaceutical composition according to claim 22 useful for the treatment of pain.

24. The pharmaceutical composition according to claim 22 useful for the treatment of migraine, depression, anxiety, schizophrenia, Parkinson's disease, or stroke.

25. A method of treating pain comprising a step of administering to one in need of such treatment an effective amount of a compound according to claim 1.

26. A method of treating migraine, depression, anxiety, schizophrenia, Parkinson's disease, or stroke comprising a step of administering to one in need of such treatment an effective amount of a compound according to claim 1.

27. A methos of treatment of glaucoma or tinitis comprising a step of administering to one in need of such treatment an effective amount of a compound according to claim 1.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/10269

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :Please See Extra Sheet.
US CL :Please See Extra Sheet.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : Please See Extra Sheet.

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS—structure
EAST/WEST—image subclass

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----- Y	US 5,648,368 A (EGBERTSON et al.) 15 July 1997, see entire article, especially column line 50-60 compound 8-5, and columns 61-62, 90-102 examples, column 3, line 12.	1-3, 22 ---------- 1-22, 24
X, P ----- Y, P	US 6,303,637 B1 (BAO et al.) 16 October 2001, see entire article especially col. 33, example 17.	1-3, 22 ---------- 1-3, 22
X --- Y	DE 3,702,755 A1 (HOESCHST AG) 11 August 1988, see entire article especially, page 18, example 23 and page 11.	1, 9-10, 22 ---------- 1, 9-12, 22
Y	WO 00/71518 (SEPRACOR, INC.) 30 November 2000, see entire document including all the examples for pages 20-49 formula A-F.	1-26

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 15 AUGUST 2002	Date of mailing of the international search report 11 SEP 2002
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer CELIA CHANG Telephone No. (703) 308-1235

Form PCT/ISA/210 (second sheet) (July 1998)★

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/10269

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X — Y	DATABASE CAPLUS on stn (Columbus, OH, USA) No. 98:191287, 'Antihypertensive 0-substituted 1-oxa-4,9-diazaspiro[5,5]undecan3-ones' abstract, Clark et al., see RN 85151-24-2.	1-3,22 1-3, 22
X, P — Y, P	DATABASE CAPLUS on STN (Columbus OH, USA) no. 135:298146, 'Dibasic inhibitors of human mast cell tryptase' abstract, Dener et al. Nov. 2001, see RN 366011-97-1.	1-3, 22 1-3, 22

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/10269

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/10269

A. CLASSIFICATION OF SUBJECT MATTER:
IPC (7):

IPC7 A61K 31/55, 31/54, 31/535, 31/505, 31/52, 31/495, 31/47, 31/44, 31/445, 31/42, 31/415, 31/425, 31/41;
C07D 223/04, 239/02, 241/02, 267/02, 401/12, 403/12, 405/12, 407/12, 409/12, 413/12, 473/12

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

514/211, 212, 235.5, 237.2, 252, 255, 256, 261, 300, 311, 312, 314, 318, 319, 326, 359, 362, 365, 374, 378, 382, 397, 403; 540/544, 609, ; 544/111, 124, 132, 242, 238, 264, 336, 360, 366; 546/113, 152, 153, 193, 208, 209, 210, 211, 212, 214; 548/134, 436, 215, 240, 255, 262.2, 338.1, 371.7, 567

B. FIELDS SEARCHED
Minimum documentation searched
Classification System: U.S.

514/211, 212, 235.5, 237.2, 252, 255, 256, 261, 300, 311, 312, 314, 318, 319, 326, 359, 362, 365, 374, 378, 382, 397, 403; 540/544, 609, ; 544/111, 124, 132, 242, 238, 264, 336, 360, 366; 546/113, 152, 153, 193, 208, 209, 210, 211, 212, 214; 548/134, 436, 215, 240, 255, 262.2, 338.1, 371.7, 567

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

Group I, claims 1-2 in part, 3, 13, 20-27 in part when NonAr is a six membered ring with one nitrogen, A is phenyl, drawn to NonAr is a six membered ring with one nitrogen, A is phenyl compounds.

Group II, claims 1-2 in part, 4, 14, 20-27 in part when NonAr is 6 membered ring with one nitrogen, A is 5-membered heteroaromatic monocyclic ring, drawn to NonAr is 6 membered ring with one nitrogen, A is 5-membered heteroaromatic monocyclic ring compounds.

Group III, claims 1-2 in part, 5, 15, 20-27 in part when NonAr is 6 membered ring with one nitrogen, A is 6-membered hetero- aromatic monocyclic ring, drawn to NonAr is 6 membered ring with one nitrogen, A is 6-membered hetero- aromatic monocyclic ring compounds.

Group IV, claims 1-2 in part, 6, 16, 20-27 in part when NonAr is a six memberred ring with one nitrogen, A is bicyclic hetero-aromatic ring drawn to NonAr is a six memberred ring with one nitrogen, A is bicyclic heteroaromatic ring compounds.

Group V, claims 1-2 in part, 7-8, 17, 20-27 in part when NonAr is 5 membered ring with one nitrogen, A is phenyl ring, drawn to NonAr is 5 membered ring with one nitrogen, A is phenyl ring compounds.

Group VI, claims 1-2 in part, 9-10, 18, 20-27 in part when NonAr is 6 membered ring with two nitrogen, A is phenyl ring, drawn to NonAr is 6 membered ring with two nitrogen, A is phenyl ring compounds.

Group VII, claims 1-2 in part, 11-12, 19, 20-27 in part when NonAr is 6 membered ring with nitrogen and oxygen, A is phenyl ring, drawn to NonAr is 6 membered ring with nitrogen and oxygen, A is phenyl ring compounds.

Group VIII, claims 1-2 and 20-27 in part when NonAr and A are the remaining variables, drawn to remaining compounds not encompassed by groups I-VII.

The inventions listed as Groups I-VIII do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the compounds of groups I-VIII differ in elements, bonding arrangements and chemical properties to such an extend that they do not share substantial commonality in structure. According to PCT Annex B of the Administrative Instruction, with respect to Markush Practice sections (f)(i)(B)(1) it was stated that the compound in a Markush description share

significant common structural element and sections (f)(i)(B)(2)(v) state however, when dealing with alternatives, if it can be shown that at least one alternative is not novel over the prior art, the question of unity of invention shall be reconsidered. Please note that the above groups I-VIII although have common elements but do not share substantial commonality in structure and also at least one alternative i.e. group VIII is not novel because Clark CA 98:191287 (see RN 85151-24-2) anticipated the group of compounds.